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ILLINOIS INSTITUTE OF TECHNOLOGY

THE CHEMISTRY OF PHOSPHETANE COMPOUNDS

BY

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Requirements for the Degree of
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Approved Sheldon Cremer
(Adviser)

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TABLE OF CONTENTS

Page

ACKNOWLEDGEMENT v

ABSTRACT vi

LIST OF ILLUSTRATIONS viii

LIST OF TABLES ix

CHAPTER

I. SYNTHESIS AND STEREOCHEMISTRY OF PHOSPHETANE DERIVATIVES 1

1. Introduction 1

2. Background 1

3. Results and Discussion 5

a. Synthesis 5

b. Reactions of Phosphetanium Salts 11

c. Reactions of Phosphetane Oxides 14

d. Stereochemistry 15

4. Experimental 26

II. STEREOCHEMISTRY OF NUCLEOPHILIC ATTACK ON CYCLIC PHOSPHORUS COMPOUNDS 49

1. Introduction 49

2. Hydrolysis of Phosphinate Esters 65

a. Results and Discussion 65

b. Experimental 74

3. Hydrolysis of Phosphonium Salts 94

a. Background 94

b. Results and Discussion 97

c. Experimental 110

TABLE OF CONTENTS - CONTINUED

Page

III. SYNTHESIS AND REACTIONS OF α-HALOMETHYLPHOSPHORUS COMPOUNDS 128

1. Introduction 128

2. Results and Discussion 130

3. Experimental 142

IV. NUCLEAR MAGNETIC RESONANCE STUDIES ON PHOSPHETANE DERIVATIVES 156

1. Introduction 156

2. Results and Discussion 157

3. Experimental 168

REFERENCES 171

VITA 178

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ABSTRACT

A series of new phosphetane derivatives (oxides, phosphinic acids, phosphinate esters, acid chlorides, etc.) was prepared by cyclization of polymethylated alkenes with phosphorus trichloride in the presence of anhydrous aluminum chloride. In addition, a number of 1-substituted 2,2,3,4,4-pentamethylphosphetane oxides were prepared by the reaction of the corresponding organometallic compound with 1-chloro-2,2,3,4,4-pentamethylphosphetane 1-oxide. Each phosphetane oxide was conveniently and stereoselectively reduced to the respective phosphetane and the latter was quaternized to give the phosphetanium salts. Ring opening reactions of phosphetane oxides and ring expansion reactions of phosphetanium salts in several systems were also investigated. A novel ring opening reaction of 1-chloro-2,2,3,4,4-pentamethylphosphetane-1-sulfide with sulfuryl chloride was observed.

The stereochemistry of nucleophilic substitution of a phosphinate ester was investigated by a detailed deuterium labelling experiment. Retention of configuration in the reaction could be rationalized by assuming the formation of trigonal bypyramid which could under go psuedorotation. Kinetics of the alkaline hydrolysis of phosphinate esters was examined. The rates in each case were second-order; first-order in each component. The rate acceleration (compared to the open-chain analogues) in these esters was explained on the basis of ease of intermediate formation resulting from strain in the ring.

Isomer crossover in phosphetanium salts was found to be catalysed by alkali. Pseudorotation of the initial intermediate was invoked as a rationale for the observed phenomenon. Phosphetanium salts were found to decompose with base stereospecifically to yield a predominance of one isomer of the oxide. The alkaline decomposition of phosphetanium salts and one phospholanium salt was investigated. The reactions were found to be third-order overall, first-order in the concentration of the phosphonium salt and second-order in alkali. Enhanced rates of hydrolysis were also observed in these cases, which corroborated the strain theory.

Reactions of α-halomethylphosphorus compound were studied to explore their potential as precursors for small-membered phosphorus heterocycles. A novel rearrangement of α-halomethylphosphines in the presence of acid was investigated in detail.

^{31}P nuclear magnetic resonance data were obtained for several phosphetane compounds. In the cases studied, no correlation could be obtained.

LIST OF ILLUSTRATIONS

Figure — Page

I-1. X-ray Data on 1-Phenyl-1,2,2,3,4,4-hexamethylphosphetanium Bromide (27) 20

I-2. Ring-puckering in 1-Phenyl-2,2,3,4,4-hexamethlyphosphetanium Bromide (27) 21

II-1. Pseudorotation in a Trigonal Bipyramid. 51

II-2. Methyltetrafluorophosphorane and Dimethyltrifluorophosphorane 53

II-3. Dimethyltrifluorophosphotane. 55

II-4. Tetramethylenetrifluorophosphorane. 56

II-5. Tetramethylenetrifluorophospherane. 57

II-6. Projection of Balaban's 20-Vertex Graph (as given by Mislow). 58

II-7. Pseudorotation in Cyclic Phosphate Esters 60

II-8. Pseudorotation in Cyclic Phosphinate and Phosphonate Esters 63

II-9. Transition States for Apical and Equatorial Departure 71

II-10. Plot of $\log(k_2/T)$ vs. 1/T for the Alkaline Hydrolysis of (11) 82

II-11. Plot of $\log(k_t/T)$ vs. 1/T for the Alakline Hydrolysis of (15) 93

II-12. Isomer Cross-over in Phosphetanium Salts by Pseudorotation. 98

11-13. Pseudorotation in Phosphetanium Salt 102

II-14. Plot of $\log(A_t-A)$ vs. time for the Alkaline Hydrolysis of (100). 113

II-15. Plot of k_{obs} vs. B^2 for the Alkaline Hydrolysis of (100). 114

III-1. Working Curve for the Estimation of Acetic Anhydride in Acetyl Chloride 153

IV-1. Plot of Calculated vs. Observed ^{31}P Chemical Shifts of Phosphetanes 162

IV-2. Pmr Spectrum of 1-Chloro-2,2,3,4,4-pentamethylphosphetane (48) 167

LIST OF TABLES

Table Page

II-1. Alkaline Hydrolysis of Phosphinate Esters. Second-Order Rate Constants at 25° 71

II-2. Alkaline Hydrolysis of Phosphinate and Phosphinate Esters 72

II-3. Alkaline Hydrolysis of 1-Methoxy-2,2,3,3,4-pentamethylphosphetane 1-Oxide (8) at 25.4°. 75

II-4. Alkaline Hydrolysis of 1-Methoxy-2,2,3,3,4-pentamethylphospnetane 1-Oxide (8) at 25.4°. 76

II-5. Alkaline Hydrolysis of 1-Methoxy-2,2,3.3,4-pentamethylphosphetane 1-Oxide (8) at 25.4°. 76

II-6. Alkaline Hydrolysis of 1-Methoxy-2,2,3,3,4-pentamethylphosphetane 1-Oxide (8) at 60°. 77

II-7. Alkaline Hydrolysis of 1-Methoxy-2,2,3,3,4-pentamethylphosphetane 1-Oxide (8) at 60°. 77

II-8. Activation Parameters for the Alkaline Hydrolysis of (8) 78

II-9. Alkaline Hydrolysis of 1-Methoxy-2,2,3,4-tetramethylphosphetane 1-Oxide (11) at 25° 78

II-10. Alkaline Hydrolysis of (11) at 25° 79

II-11. Alkaline Hydrolysis of (11) at 39.6° 79

II-12. Alkaline Hydrolysis of (11) at 39.6° 80

II-13. Alkaline Hydrolysis of (11) at 60° 80

II-14. Alkaline Hydrolysis of (11) at 60° 81

II-15. Activation Parameters for the Alkaline Hydrolysis of (1) 83

II-16. Alkaline Hydrolysis of 1-Methoxy-2,2,3,4,4-pentamethylphosphetane 1-Oxide (86) at 25°. 83

II-17. Alkaline Hydrolysis of (86) at 25° 84

II-18. Alkaline Hydrolysis of 1-Methoxy-2,2,3,3-tetramethylphosphetane 1-Oxide (15) at 0° 84

II-19. Alkaline Hydrolysis of (15) at 0°. 85

LIST OF TABLES - CONTINUED

Table | Page

II-20. Alkaline Hydrolysis of (15) at 15° 86

II-21. Alkaline Hydrolysis of (15) at 15° 87

II-22. Alkaline Hydrolysis of (15) at 25° 88

II-23. Alkaline Hydrolysis of (15) at 25° 89

II-24. Alkaline Hydrolysis of (15) at 33.9° 90

II-25. Alkaline Hydrolysis of (15) at 33.9° 91

II-26. Activation Parameters for the Alkaline Hydrolysis of (15) 92

II-27. Equilibration of Phosphetanium Salts with Base 101

II-28. Alkaline Hydrolysis of Phosphetanium Salts in 50% Ethanol-Water. Third-Order Rate Constants at 25° 107

II-29. Solvent Effect on the Hydrolysis of Phosphetanium Salts. Third-Order Rate Constants at 25° 109

II-30. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium Bromide (94) in 50% Ethanol-Water at 25° 115

II-31. Alkaline Hydrolysis of (94) in 50% Ethanol Water at 50°. 116

II-32. Alkaline Hydrolysis of (94) in 50% Ethanol-Water at 50°. 116

II-33. Alkaline Hydrolysis of (94) in 50% Ethanol-Water at 25°. 117

II-34. Activation Parameters for the Alkaline Hydrolysis of (94) in 50% Ethanol-Water 117

II-35. Alkaline Hydrolysis of 1-Phenyl-1,2,2,3,3-pentamethylphosphetanium Bromide (102) in 50% Ethanol-Water at 25° 118

II-36. Alkaline Hydrolysis of (102) in 50% Ethanol-Water at 25° 118

II-37. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium Bromide (100) at 25.2° 119

II-38. Alkaline Hydrolysis of (100) at 25.2° 119

LIST OF TABLES - CONTINUED

Table Page

II-39. Alkaline Hydrolysis of (100) 120

II-40. Alkaline Hydrolysis of (100) at 39.6° 120

II-41. Alkaline Hydrolysis of (100) at 60° 121

II-42. Alkaline Hydrolysis of (100) at 60° 121

II-43. Activation Parame for the Alkaline Hydrolysis of (100). 122

II-44. Alkaline Hydrolysis of 1-Benzyl-1,2,2,3,4,4-hexamethylph 122

II-45. Alkaline Hydrolysis of 1,1-Dibenzyl-2,2,3,4,4-pentamethylphosphetanium Bromide (26). in 50% Ethanol-Water at 25° 123

II-46. Alkaline Hydrolysis of 1-Phenyl-1,2,2,3,4,4-hexamethylphosphetanium Bromide (27) in 50% Ethanol-Water at 25° 123

II-47. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-2,2, 3,4,4-pentamethylphosphetanium Bromide at 25°. 124

II-48. Alkaline Hydrolysis of (94) in 50% Ethanol-Water at 25° 124

II-49. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium Bromide (100) in queous Solution at 25°. 125

II-50. Alkaline Hydrolysis of (100) in 50% Ethanol-Water at 25° 125

II-51. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-2,2,3, 3,4-pentamethylphosphetanium Bromide (101) in Aqueous Solution at 25°. 126

II-52. Alkaline Hydrolysis of (101) in 50% Ethanol-Water at 25° 126

II-53. Alkaline Hydrolysis of 1-Phenyl-1,2,2,3,3-pentamethylphosphetanium Bromide (102) in 50% Ethanol-Water at 25° 127

II-54. Alkaline Hydrolysis of 1-Benzyl-1-phenyl-phospholanium Bromide (104) in 50% Ethanol-Water at 25° 127

LIST OF TABLES - CONTINUED

Table		Page
III-1.	Relative Rates of Nucleophilic Substitution in α-Halomethyl Compounds	136
III-2.	Results of NMR Integration of Labelling Experiments for Chloromethyldiphenylphosphine	151
III-3.	Kinetics of Halogen Exchange of the Reaction of $Ph_2P(O)-CH_2Cl$ I	155
IV-1.	^{31}P Chemical Shifts of Phosphetanes, Relative to 85% H_3PO_4	161
IV-2.	^{31}P Chemical Shifts of Phosphetanium Salts Relative to 85% H_3PO_4	165
IV-3.	^{31}P Chemical Shifts of Phosphinate Esters Relative to 85% H_3PO_4	166

CHAPTER I

SYNTHESIS AND STEREOCHEMISTRY OF PHOSPHETANE DERIVATIVES

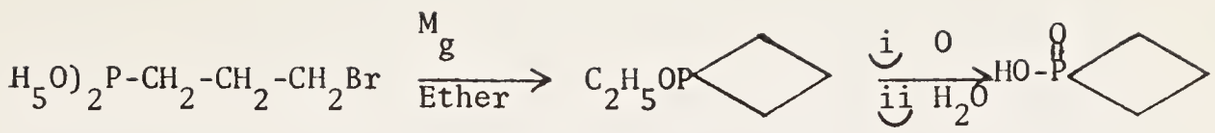
1. Introduction

Small-membered phosphorus heterocycles have attracted considerable attention, not only in the area of their synthesis [1,2] but also from the point of view of their stereochemistry, chemical reactivity [2], and physical properties. The chemistry of phosphetane (phosphacyclobutane) systems has been investigated in detail; interestingly, a number of the reactions seem to occur by initial attack at the phosphorus site. These phosphetanes, in general, have contributed significantly to the knowledge of phosphorus chemistry because they undergo reactions and possess physical properties which are unique to the four-membered ring system and are quite different than those observed in open-chain analogues.

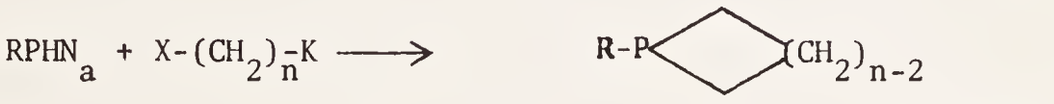
2. Background

The general methods for the preparation of these phosphorus heterocycles have been reviewed [2,3]. However, it is pertinent to briefly describe the various methods of synthesizing four-membered phosphorus heterocycles.

Kosolapoff [4] has measured the pK_a of a four-membered cyclic phosphinic acid. The synthesis involving an intramolecular Grignard reaction, resulted in a very poor yield (0.1%) and therefore was of little preparative value.



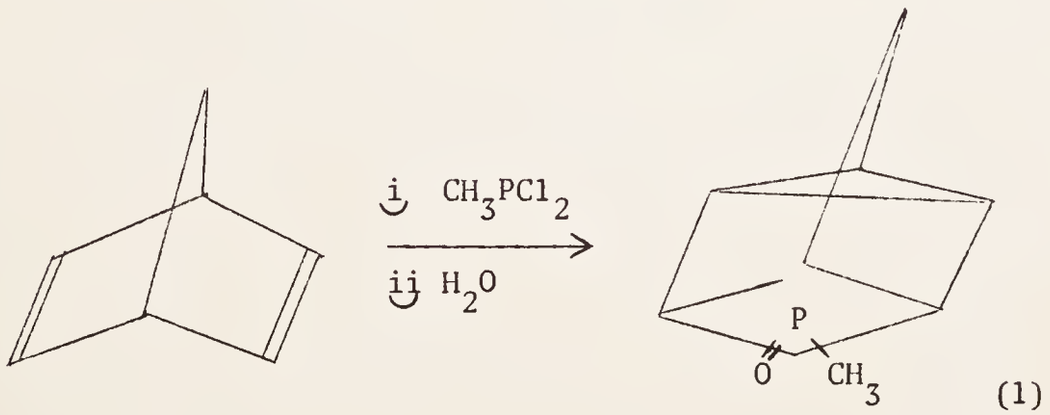
A general method for the synthesis of phosphorus heterocycles has been described by Wagner [5,6,7] in which a sodium alkylphosphinide is allowed to react with an α,ω - dihaloalkane. Phosphetane systems result when n=3 in the following equation:



n= 2 to 7.

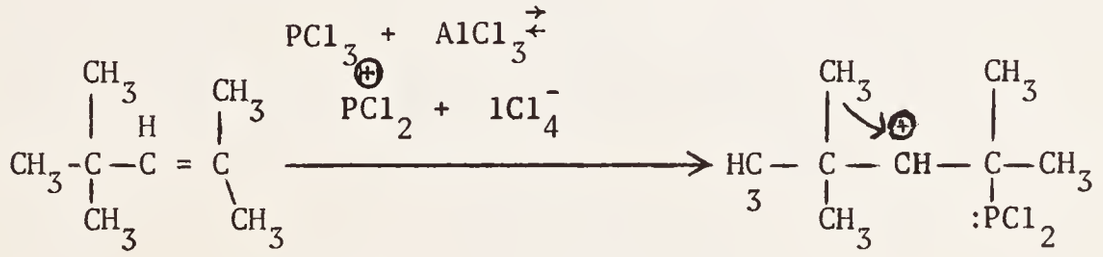
Unfortunately, this method has been reported in the patent literature only, and the experimental details of these synthesis have not been given.

Green [8] has described the synthesis of a four-membered ring in a tricyclic system (1). The preparation consists of the conjugate addition of methylphosphonous dichloride to norbornadiene. However, attempts to repeat this reaction have been unsuccessful [9].



(1)

The synthesis of a highly methylated phosphetane derivative has been described by McBride and co-workers [11]. The preparation was accomplished by the treatment of 2,4,4-trimethyl-2-pentene with a complex of phosphorus trichloride and anhydrous aluminum chloride in methylene chloride solution. The propesed mechanism involves electrophillic attack of the phosphorus moiety (PCl_2^+) on the double bond of the alkene. The resultant secondary carbonium ion (2) undergoes a Wagner-Meerwein rearrangement in which one of the terminal methyl groups tertiary carbonium ion (3) as indicated in the following scheme. The latter cyclizes to produce the phosphonium salt (4) which on treatment with water gives the acid chloride (5). The intermediacy of (4) has been verified in the nmr by Cremer [9].



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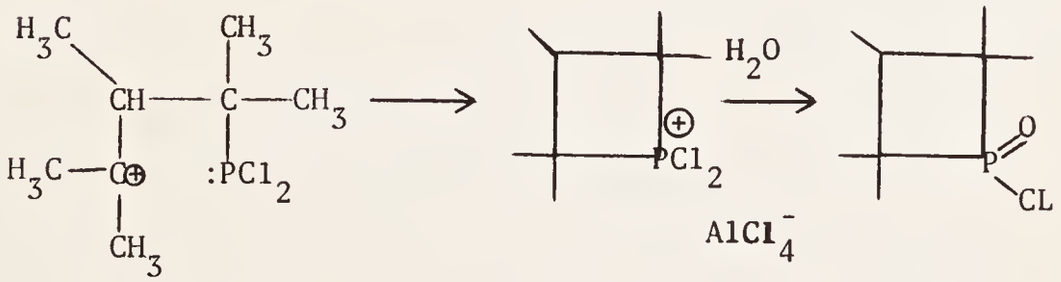
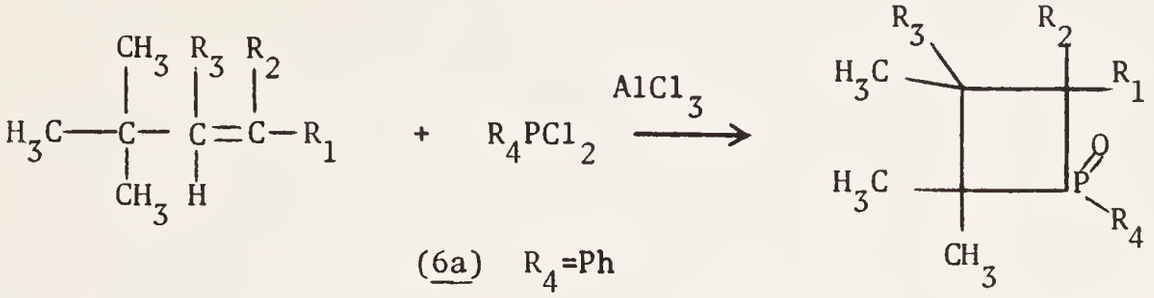


(3) (4) (5)

The above preparation has subsequently been extended by Cremer and Chorvat[11] for the synthesis of a number of substituted phosphetane compounds by using phenyl-phosphonous dichloride (6 a) and methylphosphonous dichloride (6 b). A variety of substituted alkenes were employed as well. The illustration below summarizes their results:



(6a) R_4=Ph

(6b) R_4=CH_3

i) R_1=R_2=CH_3, R_3=H, R_4=Ph

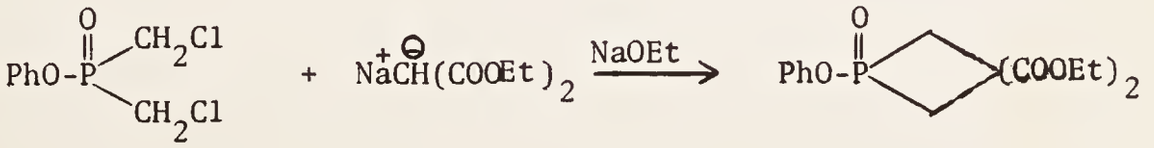
ii) R_1=R_2=CH_3, R_3=H, R_4=CH_3

iii) R_1=CH_3, R_2=H, R_3=CH_3, R_4=Ph

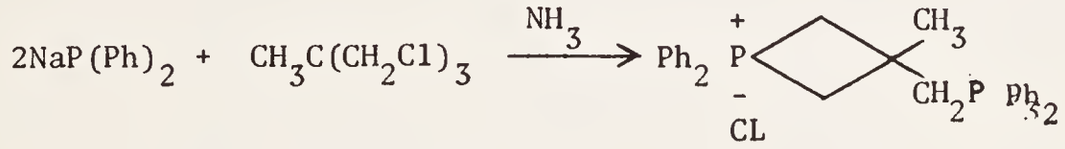
iv) R_1=R_2=H, R_3=CH_3, R_4=Ph

v) R_1=R_2=R_3=H, R_4=Ph

Recently, Zyablikova and co-workers[12] have described the preparation of phosphetane oxides by the treatment of phenyl bis-(chloromethyl) phosphinate with the sodium salt of diethyl malonate in the presence of sodium ethoxide. The product is the result of a double displacement reaction:

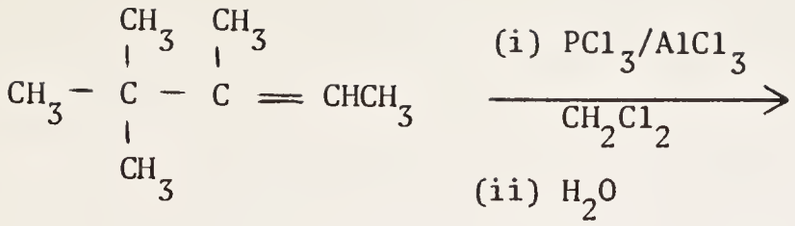


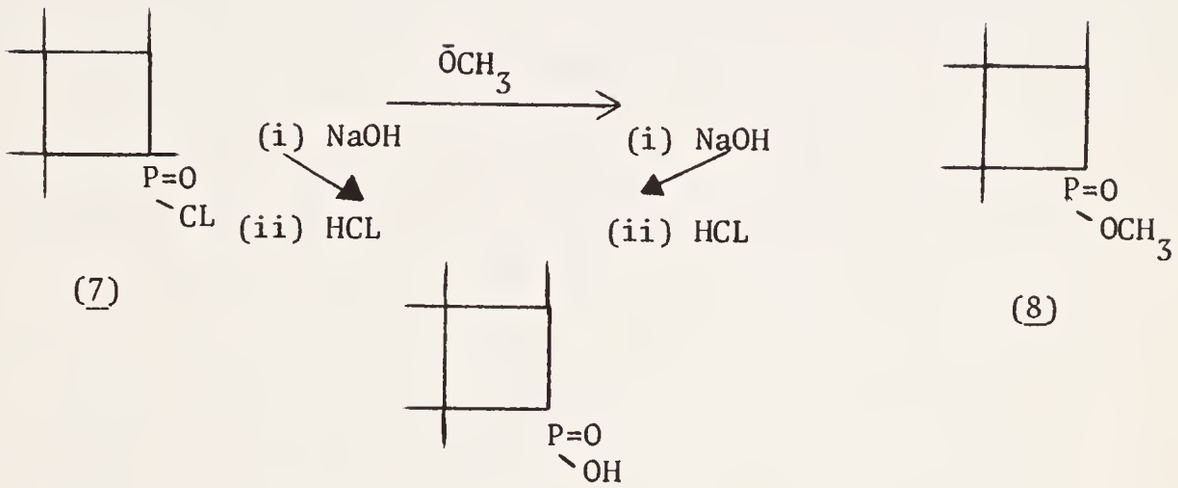
The corresponding carboxylic acid was produced by hydrolysis and decarboxylation of the product. Another recent example of the syntheses of a phosphetane derivative has been provided by Berglund and Meek [13]. Ring formation was achieved by treating 2-chloromethyl-2-methyl-1,3-dichloropropane with sodium diphenylphosphide in liquid ammonia to produce a substituted phosphetanium salt:



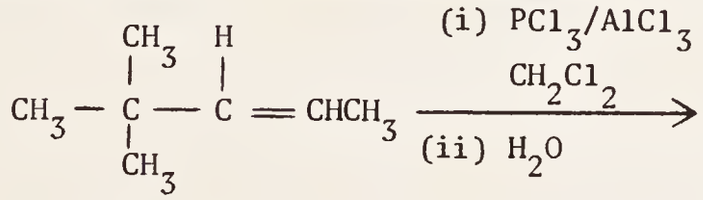
3. Results and Discussion

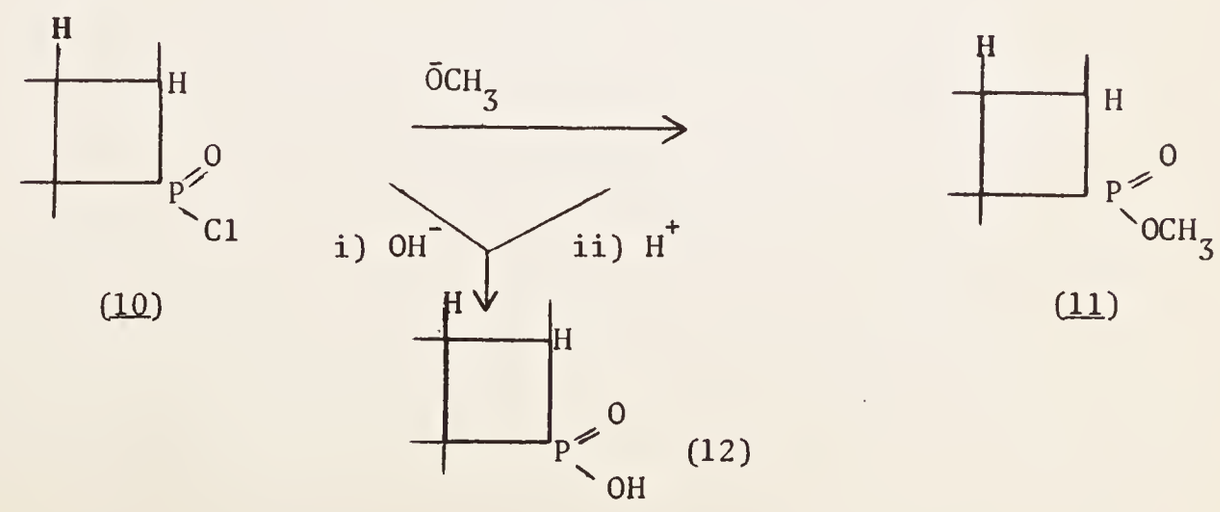
a) Synthesis. This phase of the project consisted in the synthesis of new phosphetane compounds and involved the study of the chemical reactivity and the physical properties of these as well as other reported compounds. The method of McBride [10] which was extended by Cremer and Chorvat [11], was utilized for the preparation of various new acid chlorides. Thus, addition of 3,4,4-trimethylpentene-2 to a previously prepared complex of PCl_3/ $AlCl_3$ in methylene chloride solution followed by the decomposition of the resultant solution with water yielded 1-chloro-2,2,3,3,4-pentamethylphosphetane 1-oxide (7). Treatment of the latter with sodium methoxide gave the corresponding phosphinate ester (8). Both (7) and (8) could be hydrolyzed to the acid (9) with alkali:





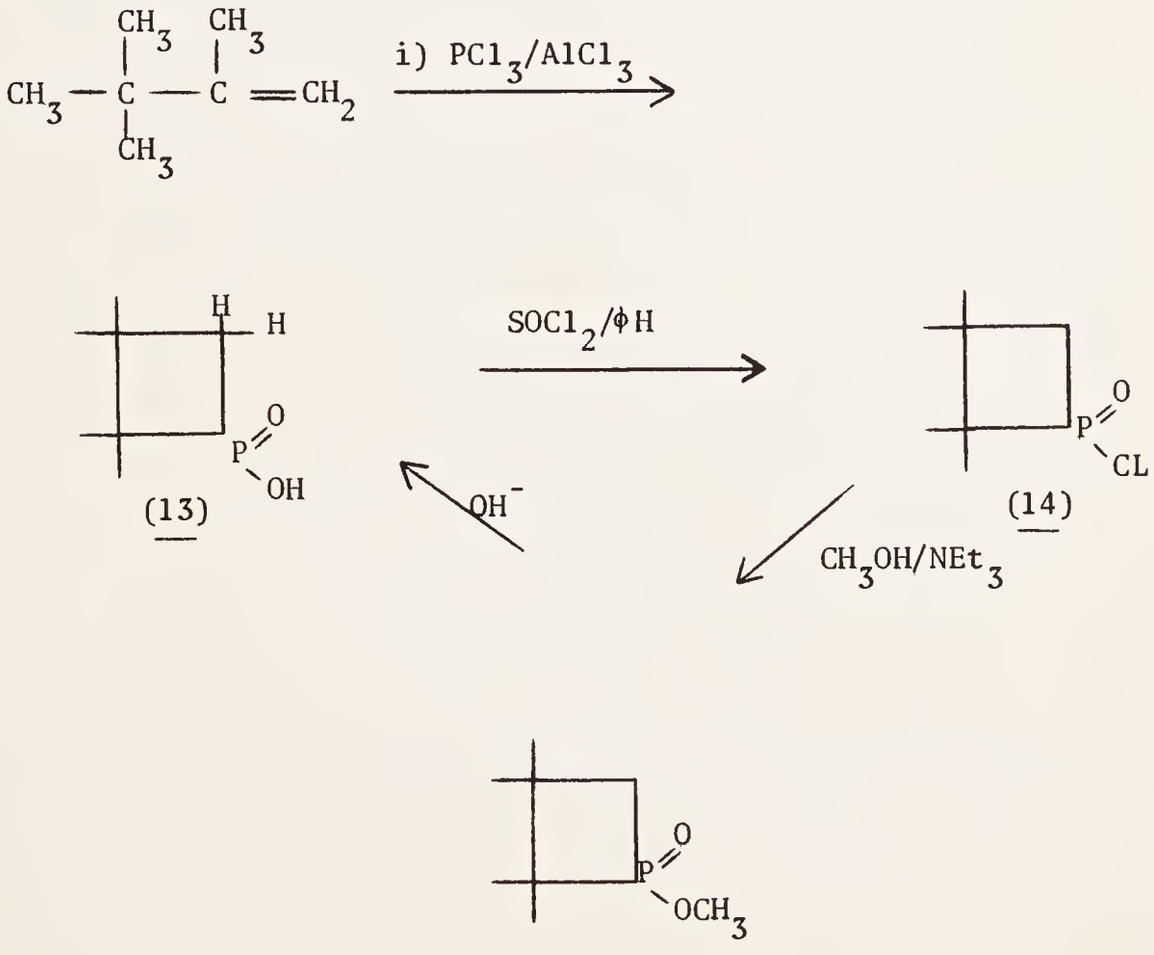
Similarly, 1-chloro-2,2,3,4-tetramethyl 1-oxide (10) was prepared starting with 4,4-dimethyl-2-pentene-2; the resultant acid chloride (10) was converted to the corresponding ester (11) and acid (12):



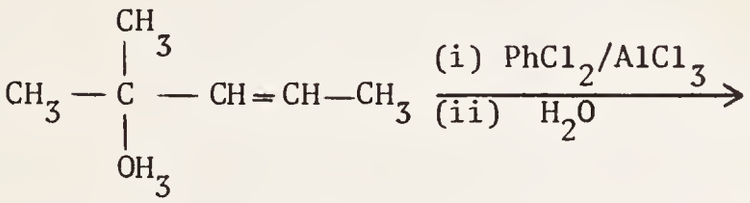


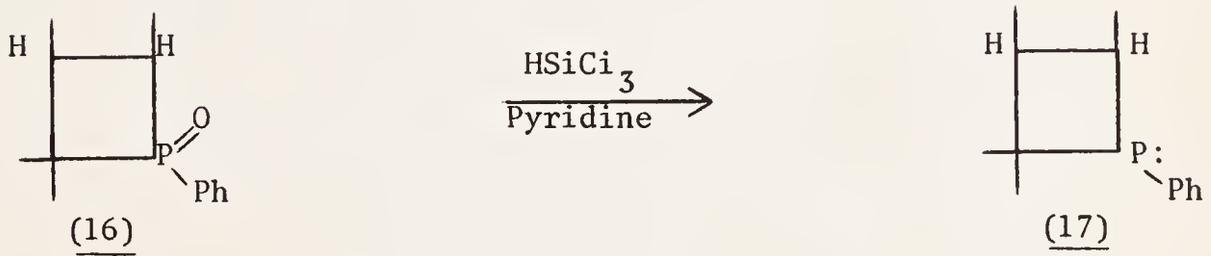
It may be noted here that although compound (11) contains three asymmetric centers, predominantly one isomer of the product was obtained (determined by nmr). Thus, the ring closure seems to occur in a highly stereoselective manner.

Because of the sensitivity of 1-chloro-2,2,3,3-tetramethylphosphetane 1-oxide (14) produced from 2,3,3-trimethylbutene-1) to water, it was not possible to isolate this material. The ester derivative (15) was readily obtained by treatment of crude (14) with methanol-triethylamine (15). The acid (13) was obtained by the alkaline hydrolysis of (15) . The acid in turn could be converted to the acid chloride (14) with thionyl chloride.



The cyclization reaction described above, was extended to the synthesis of 1-phenyl-2,2,3,4-tetramethyl-phosphetane 1-oxide (16) as well as a fused system (19). The former was prepared by the treatment of 4, 4-dimethylpentene-2 with $PhPCl_2/AlCl_3$. Reduction of (16) with trichlorosilane pyridine yielded the phosphetane (17) which was quaternized to give the salt (18):





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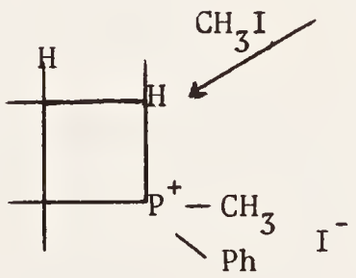
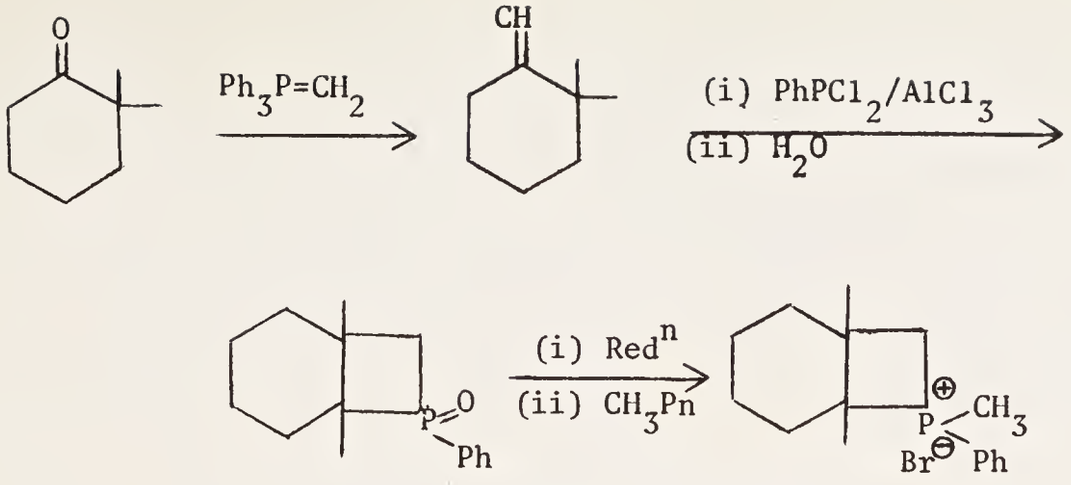


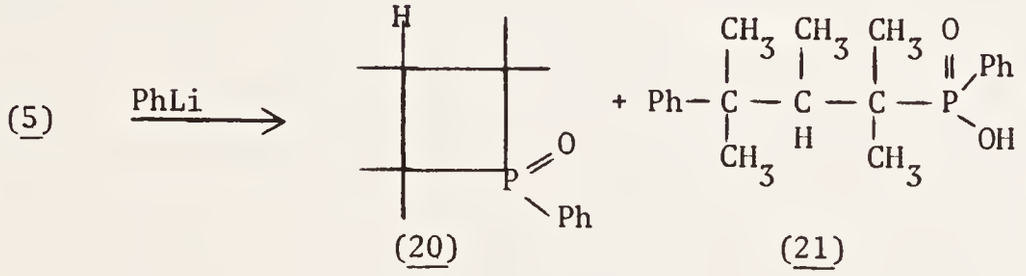
(18)

The fused system (19) was synthesized by the following procedure; the synthesis of the precursor is also illustrated:



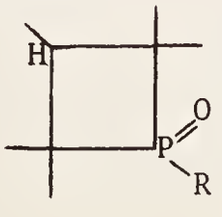
(19)

Cremer and Chorvat[11] had investigated the reaction of phenyllithium with (5) and isolated the corresponding phenylphosphetane oxide (20) with the open-chain oxide (21):



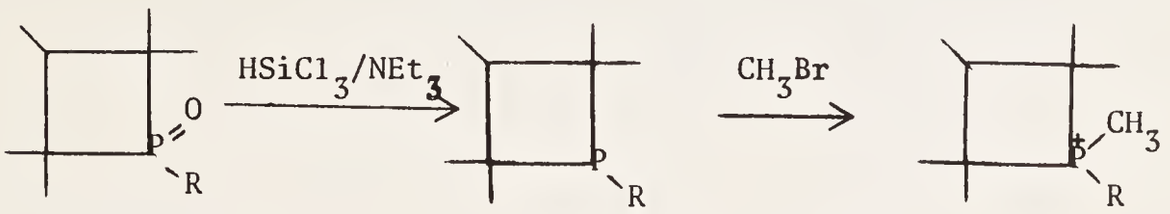
(20) (21)

The reaction of organometallic reagents with the acid chloride (5) was generalized to include other alkyl and aryl substituents at the phosphorus heteroatom. Treatment of (5) with the appropriate Grignard reagent or organolithium compound gave a number of phosphetane oxides; the reaction proceeded with high stereoselectivity to give only one isomeric product in each case:

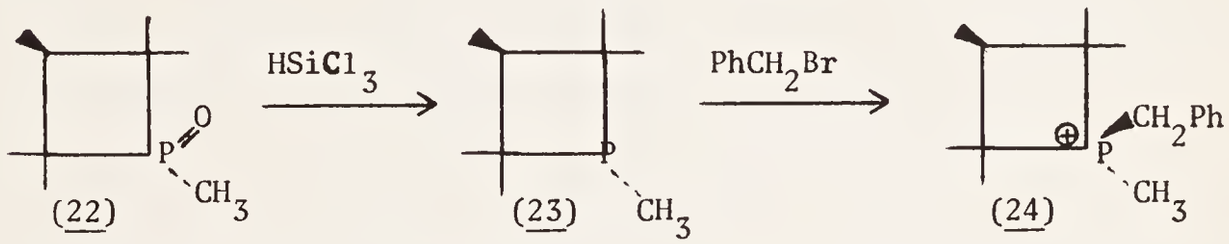


R = $-CH_2Ph$, 1-naphthyl, 1-phenanthryl,
9,-phenanthryl, $-CH_3$ (9), t-Butyl (14)
m & p - chlorophenyl, (14), p - fluorophenyl (14).

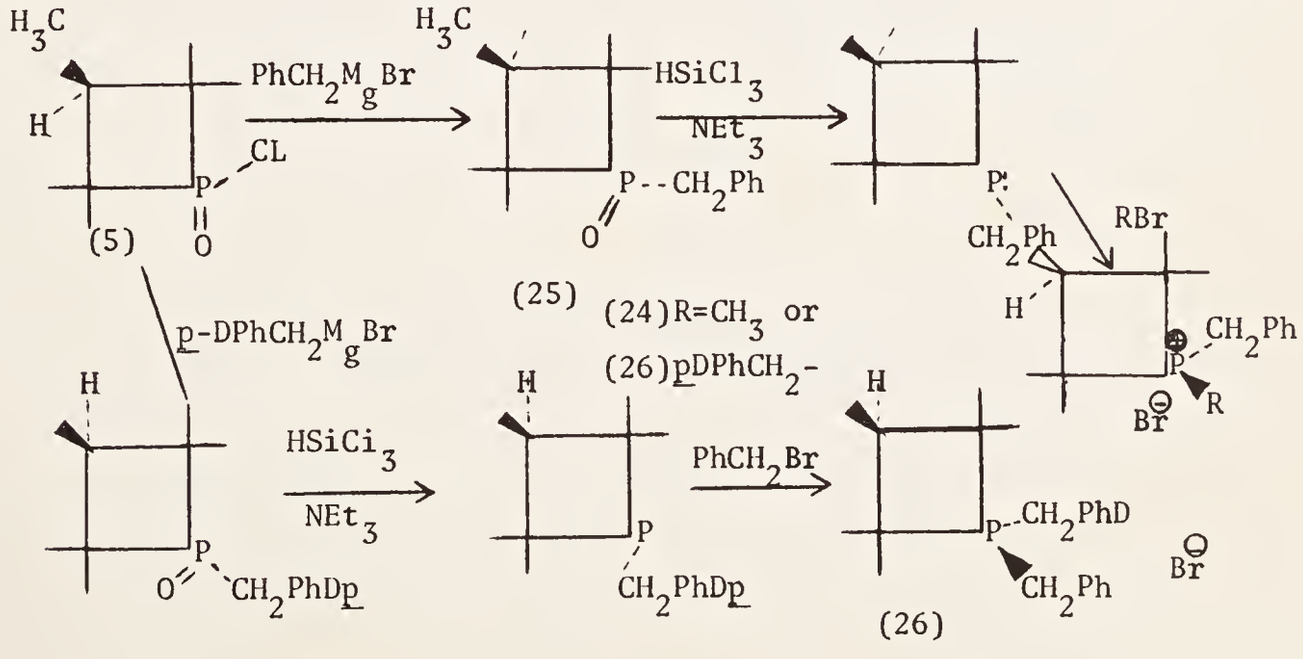
The stereospecific reduction of the phosphine oxides with trichlorosilane/triethylamine gave the corresponding phosphetanes. Quaternization of the phosphetanes with methyl bromide gave the quaternary salts:



One stereoisomer of the salt (24) (R=benzyl) was prepared (12) by the reduction of the methylphosphetane oxide (22) followed by quaternization of the phosphine (23) with benzyl bromide (for stereochemistry see p.15):

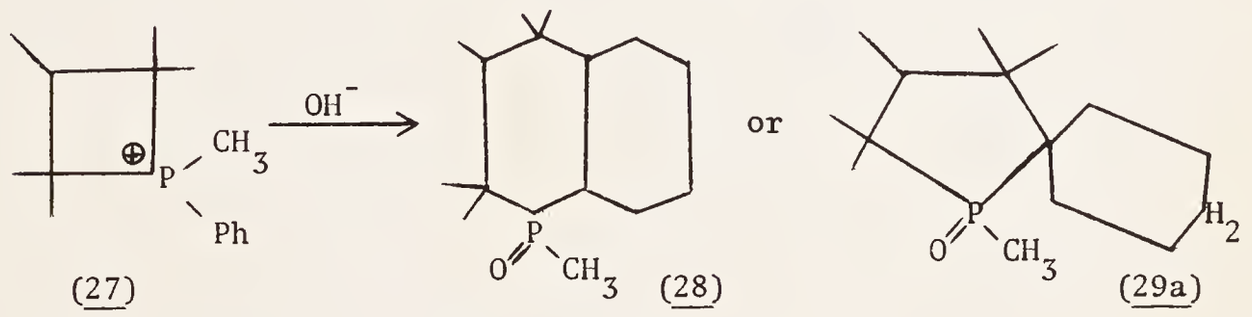


The synthesis of the benzylphosphetane oxide (25) made the preparation of the other isomeric salt possible, as shown below. Two isomers of the p-deuteriobenzyl salts were also prepared by the same method:

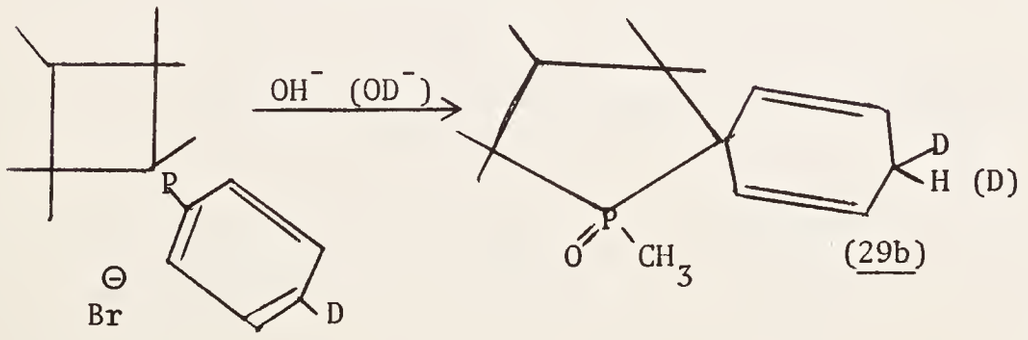


These salts have been very useful for studying the participation of pseudorotation in these systems.

B. Reactions of Phosphetanium Salts. The alkaline decomposition of the phosphonium salt (24) was also investigated by Cremer and Chrovat[15]. The initial structure (28) for the product was found to be incorrect and was later assigned the new structure (29) by Cremer [17] by using a deterium labelling experiment. Cremer treated 1-p-deuteropheny1-1,2,2,3,4,4-hexamethyl-phosphetanium bromide (30)with alkali and observed that the deuterium atom in the product was at the allylic position as shown in structure (29b) rather than the vinylic position as would be the case if structure (28) was correct. Treatment of (30) with NaOD gave the corresponding dideuterio compound which showed no allylic protons in nmr:



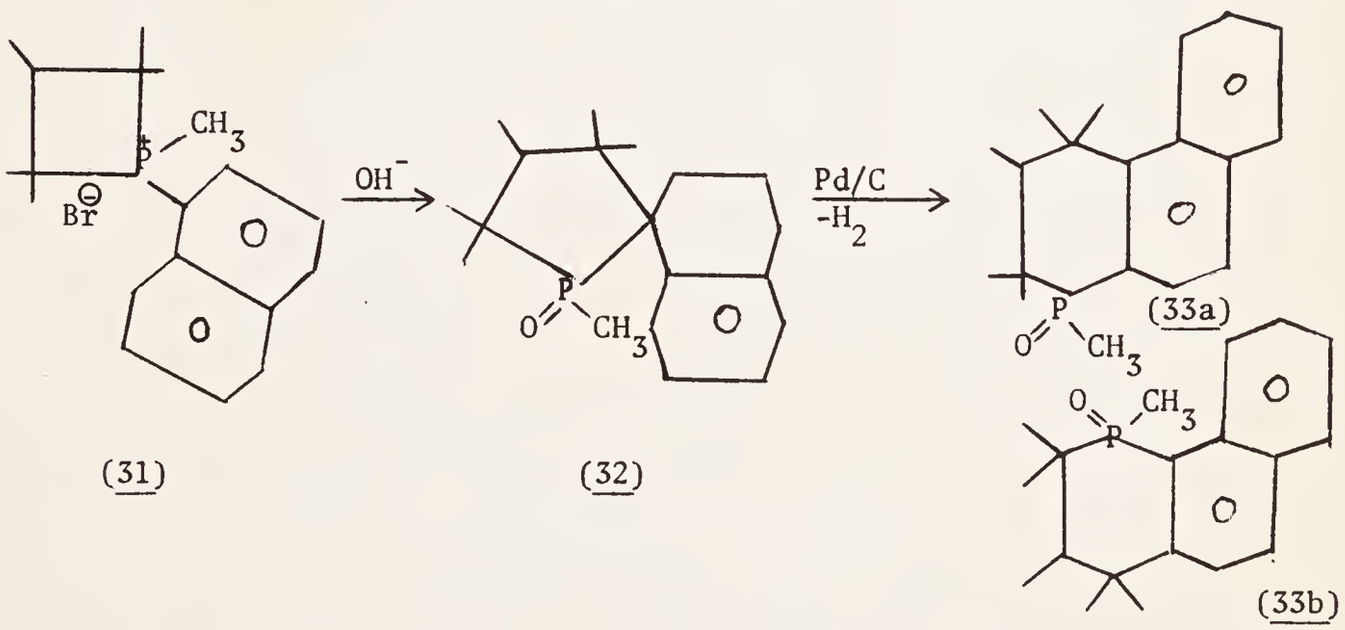
(27) (28) (29a)



(30) (29b)

Recently, Tripett and co-workers [18] have arrived at similar conslusions.

The unique rearrangment reaction observed from the decomposition of the salt (27) has been extended to the synthesis of various tri and tetracyclic phosphorus compounds. Compound (31) for instance, was decomposed to the tricyclic phosphine oxide (32). Aromatization of the latter by Pd/C dehydrogenation (19) would result in the cleavage of one of the bonds to yield either of the two isomeric phosphine oxides; compound (33a) would result from the cleavage of a P-C bond whereas (33b) would result from the breakage of a C-C bond.



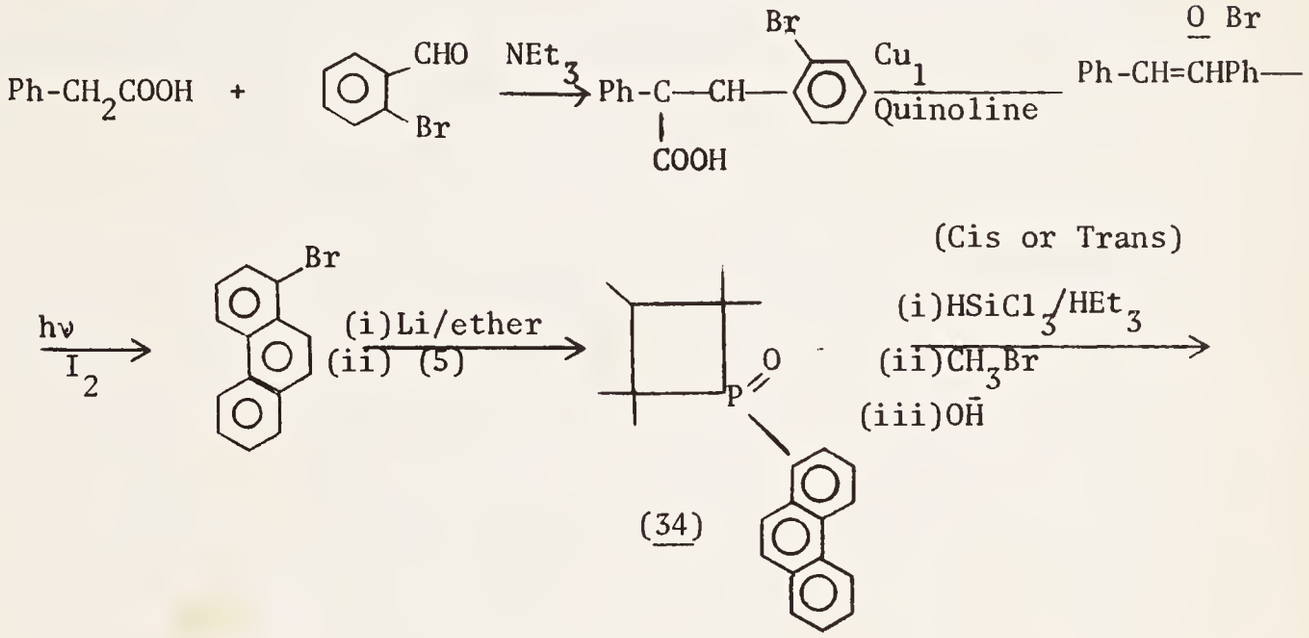
(31) (32) (33a) (33b)

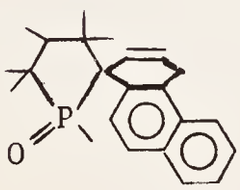
The rearrangement during aromatization is not without precedent (20):

Since there is little difference between the bond energies of the P-C bond (80 kcal.) (21) and the C-C bond (77-80 kcal.) (22); it would be difficult

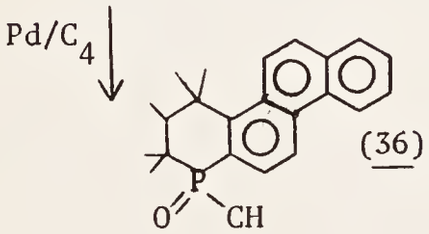
to predict which of the products (33a or b) would predominate.

In any event, these compounds are potential precursors for steroid-like molecules containing phosphorus atoms at either the 1- or 4-position; to date "phosphasteroids" are an unknown class of compounds. The tetracyclic model precursor (36) of the steroidal skeleton was prepared in the following manner;





(35)



(36)

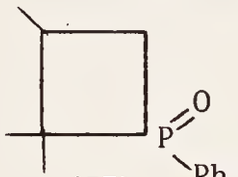
C. Reactions of Phosphetane Oxides. Alkaline decomposition of tertiary phosphine oxides results in the formation of a phosphinic acid and a hydrocarbon (23):

$$R_3P{=}O + \bar{O}H \longrightarrow R_2P(O)\text{-}OH + RH$$

As would be anticipated, the leaving group which stabilizes a negative charge should be the easiest to remove (24).

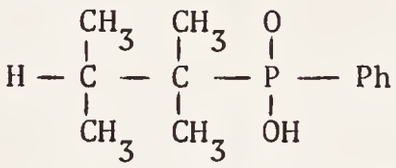
$$PhCH_2 > Ph^- > CH_3 > \text{higher alkyls.}$$

However, alkaline treatment of 1-phenyl-2,2,3-trimethylphosphetane 1-oxide (37) resulted in the ring-opened compound (38):



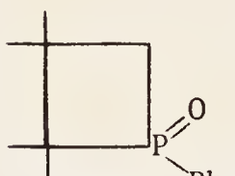
(37)

$\xrightarrow[\text{methyl cellosolve}]{OH^-}$



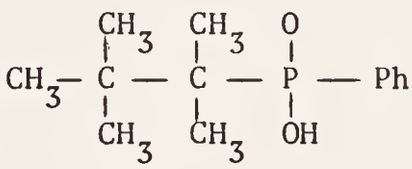
(38)

Similarly, 1-phenyl-2,2,3,3-tetramethylphosphetane 1-oxide (39) gave an open chain phosphinic acid (40) on treatment with alkali:



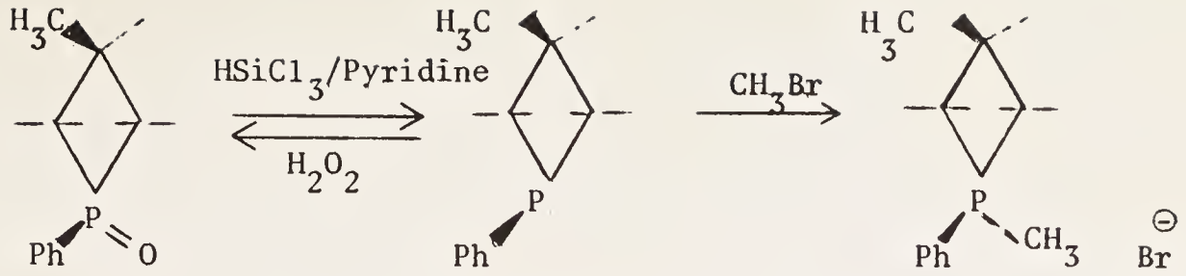
(39)

$\xrightarrow[\text{methyl cellosolve}]{OH^-}$



(40)

The results above are surprising, since on the basis of carbanion stability, one would anticipate the formation of benzene. The ring-opening during alkaline decomposition, therefore, reflects the strain in the four-membered ring.



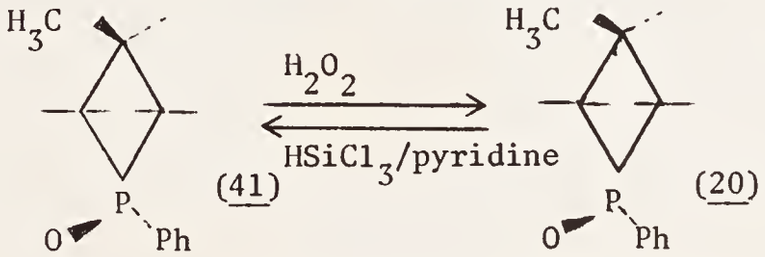
(20) (41) (27)

Stereochemistry. The stereochemistry involved in the preparation of the four-membered ring compounds as well as that of the reactions of these heterocyclic compounds has stimulated considerable research in this laboratory and other [1,14,17]. Cremer and co-workers [11] first prepared the phosphetane oxide (20) and assigned the cis- (1-phenyl and 3-methyl) geometry to the high melting isomer (126-127°). The other isomer which melts at 117-118° has also been isolated. The original (tentative) assignment was based on the fact that the oxide (20) underwent stereoselective reduction with trichlorosilane/pyridine [25] to give a phosphetane (41). The latter was assigned cis-geometry on the basis of nmr studies as well as thermodynamic equilibrium work [26]. The phosphetane (41) was subsequently quaterized with methyl bromide to yield a salt which was submitted for X-ray analysis. The 3-methyl and 1-phenyl groups were shown to have a trans relationship [27](*). Since the quaternization step is known to proceed with retention of configuration [28] at the phosphorus, the assigned geometry of the phosphetane was not substantiated. Hydrogen peroxide oxidation of the phosphetane(41) gave back the starting isomeric phosphetane oxide (20). Since this oxidation is known to proceed with retention of configuration[29] it was concluded that the oxide (20 - high melting) possessed the trans geometry.

(*) Prof. Trefonas, Private Communication. Prof. Trefonas has revealed that the geometry is trans; although it is shown cis in this publication[27].

The rigorous assignment of the phosphetane oxide however, has been subject to some confusion. An original communication of Caughlan and Haque [30] referred to the oxide (m.p. 127°) [20] as "cis" but pictorially represented the substituents in the trans configuration. Caughlan has recently disclosed that the "cis" assignment was incorrect and that the molecule is the "trans" isomer [29]. Trippett has made several unwarrented assumptions with respect to Caughlan's X-ray work and has written reversed geometry in several publications.

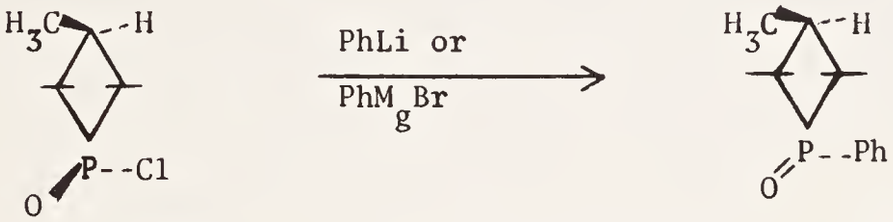
The above mentioned X-ray data of Caughlan [30] and Trefonas [27] necessarily led to the following stereochemical course of the reduction and oxidation reactions. As illustrated below, the reduction with trichlorosilane as well as the oxidation with hydrogen peroxide must proceed with retention of configuration to account for the X-ray results:



Recently, Haque[32] has performed an X-ray analysis on compound (5) and has shown that the chloro-substituent at the phosphorus and the methyl group at position 3 have a trans relationship.

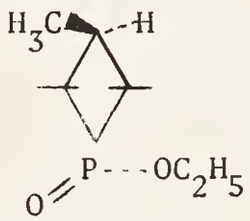
(5)

The acid chloride (5) can be converted to the phenyl-phosphetane oxide (20, m.p. 127°) by treatment with phenyl-lithium or phenylmagnesium bromide [2]. Since the oxide (20) has been shown to be the trans isomer, the reaction with organometallic reagents must proceed with retention of configuration at the phosphorus:



(5) (20)

In view of the above discussion, it seems reasonable to conclude that treatment of the trans acid chloride (5) with sodium methoxide should also yield the trans ester (42) via a retention mechanism [33] (*). This assignment is consistent with that of Bergesen's [34] who claimed to have isolated both the isomers of the analogous ethyl ester. He assigned the stereochemistry on the basis of refractive index, desity and nmr data.



The X-ray investigations [27,30] mentioned above, have not only provided the geometrical relationship of substituents but also data on the bond-lengths and bond angles in the phosphetane system. Fig. 1 represents one such system [27]. The strain in the molecule is evident from the internal angles in the ring in which the angles are C_2-P-C_4 = 82.6°, P-C_2-C_3 = 83.9°, and P-C_4-C_3 = 85.4°. The angles between the substituents external

(*) This has been substantiated by a detailed labelling study (p.67).

to the ring at the phosphorus is nearly tetrahedral (109.1°) The bond length data, however, is rather striking. The P-C bonds in the ring are slightly longer (1.90 and 1.94 Å) than the reported values in other systems (1.78-1.84 Å) [21].

The C-C bond lengths for the ring (1.60 Å) are longer than theoretical values; this also appears to be the case for the C-CH_3 bonds at positions 2 and 4. The bond length C_3-CH on the other hand is very short (1.36 Å). This shortening of the C-C bond distance has been shown not to be due to crystal packing.

Another interesting feature of the ring system is the puckering of the four-membered ring. The phosphetane ring has been shown to be nonplanar with a dihedral angle of 24°. This has also been found to be the case in compound (5) [32]. All pertinent data are shown in the Fig. 1. The puckering seems to be in the predictable direction in Fig. 2 because in that conformation, the nonbonded interactions would probably be minimal.

As mentioned earlier (p. 3), a symmetrical intermediate (4) is formed during the synthesis of the acid chloride (5). Stereoselective hydrolysis gives a predominance of the trans isomer of (5). This stereoselectivity can be rationalized on the basis of the following assumptions [35]:

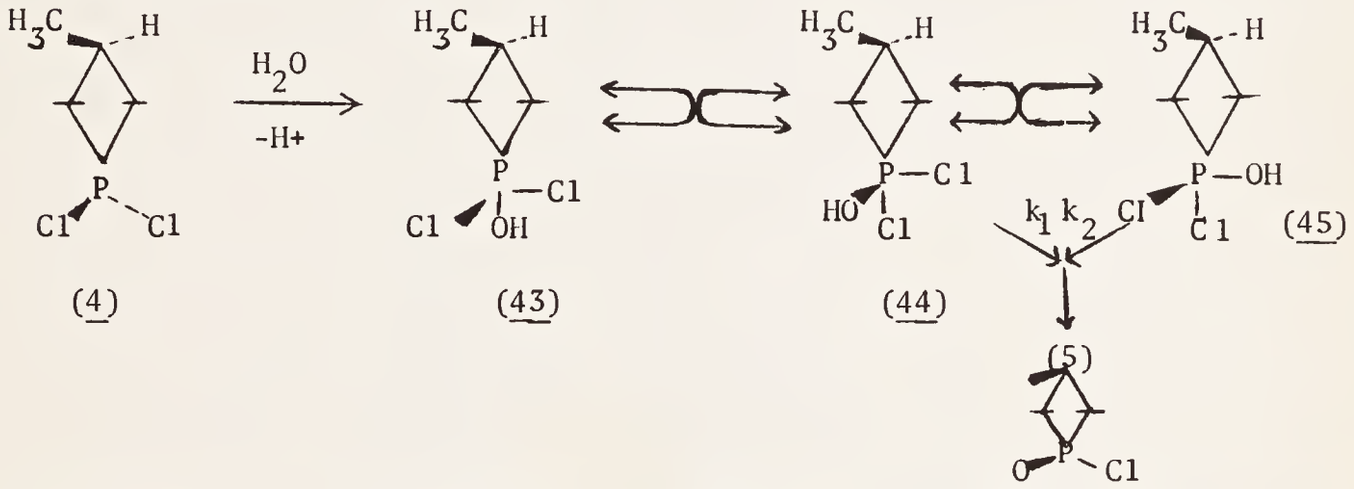
i) a pentacovalent intermediate is formed by an apical attack of water which is similar to that formed during the alkaline hydrolysis of phosphonium salts (see p. 98),

ii) the intermediate phosphorane is capable of undergoing pseudoration (see p. 98),

iii) the leaving group departs from an apical position only.

Attack of a molecule of water on the symmetrical intermediate (4),

followed by loss of a proton gives the phosphorane intermediate (43) Pseudorotation of the latter would yield two other phosphoranes (44) and (45) both of which are capable of undergoing decomposition by the loss of chloride ion from the apical position, followed by the loss of a proton to yield (5). In intermediate (44), the solvated hydroxy group is on the same side of the ring as the 3-methyl group. An interaction of these two groups would result in the faster decomposition of (44) than (45)(i.e.$k_1 \quad k_2$ in the scheme below):



A similar explanation can be advanced for the stereoselective formation of one predominant isomer of the phenylphosphetane oxide (20) during an alkaline decomposition of the corresponding benzylphosphetanium salt. This reaction occurs without ring opening; there is no departure of the apical P-C bond.

The above argument staisfactorily explains the formation of tne isomer of the acid chloride (5). Bergesen [34] has described the isolation of the single isomer of (5). McBride [11] in his original paper has made similar claims. Thionyl chloride treatment of the acid (46) rendered a mixture of isomeric acid chlorides (5) which are quite distinct in the nmr [33]. This is more reasonable in view of the tautomerization of the acid in solution:

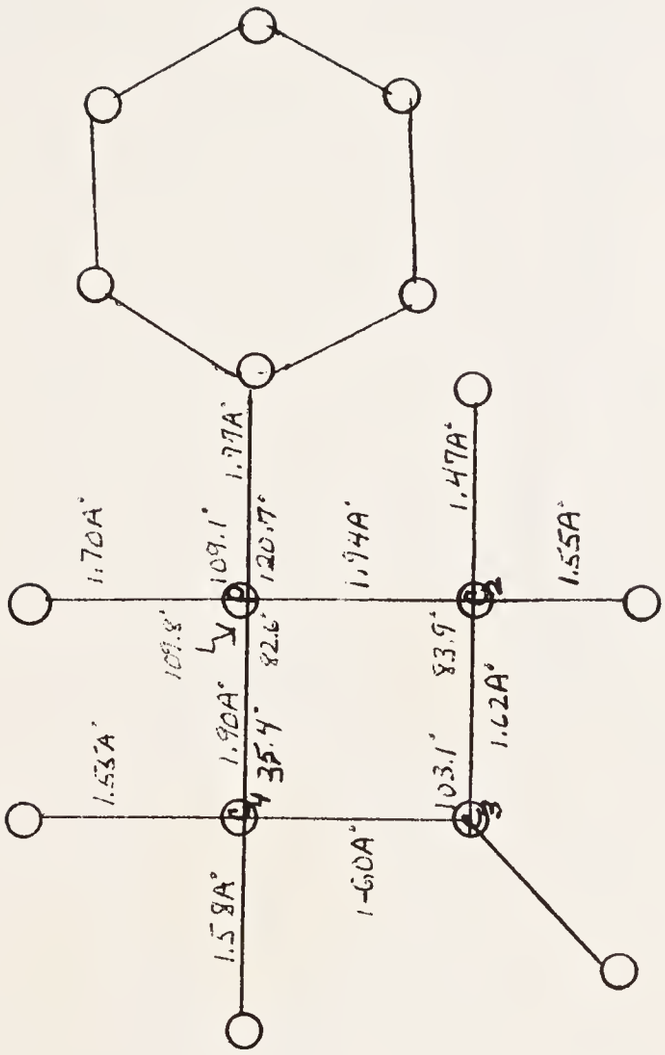

1.70A°
109.1°
1.97A°
120.7°
1.514A°
1.47A°
1.55A°
109.8°
82.6°
83.9°
1.53A°
1.90A°
35.4°
103.1°
1.62A°
1.60A°
1.58A°

Fig. I-1.

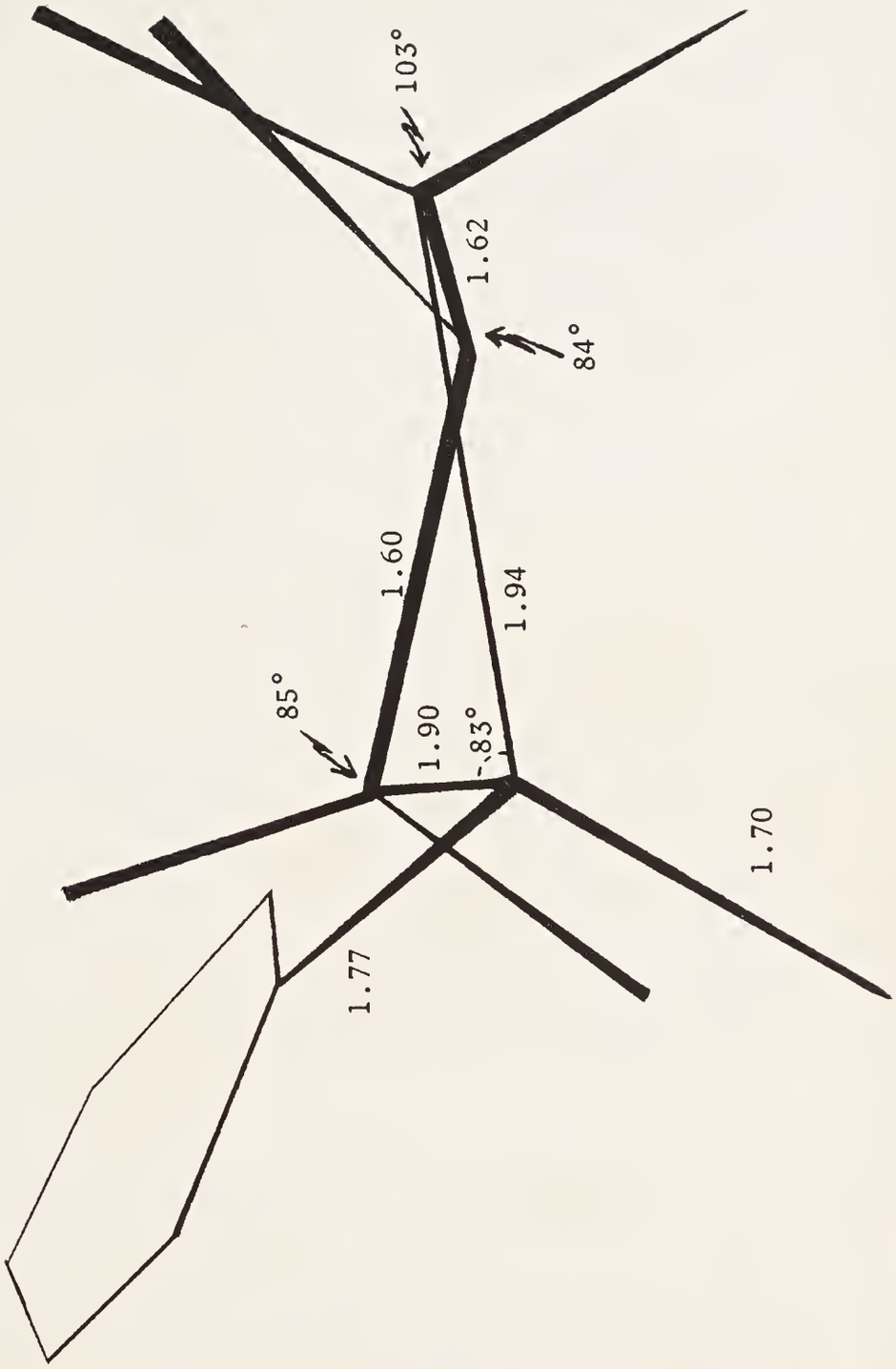
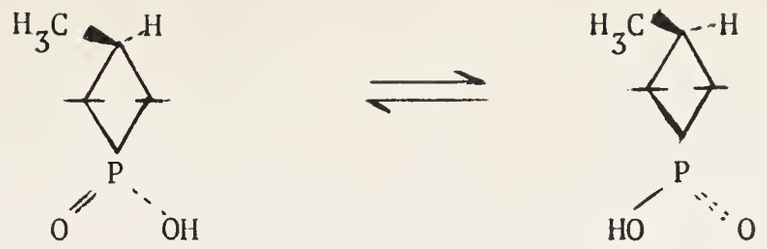
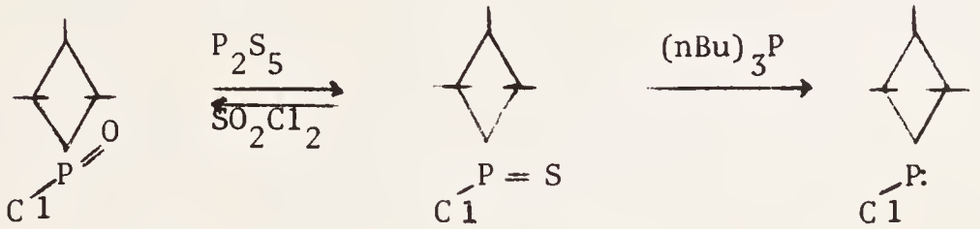


Fig. I-2. Ring-puckering in 1-phenyl-1,2,2,3,4,4-hexamethylphosphetanium bromide (27). The cis (1-phenyl+3-methyl) is shown.



(46)

To obtain conclusive proof for the stereochemical course of various reactions, it was critical to synthesize the cis isomer of the acid chloride (5). One possible approach was based on the following sequence of reactions:

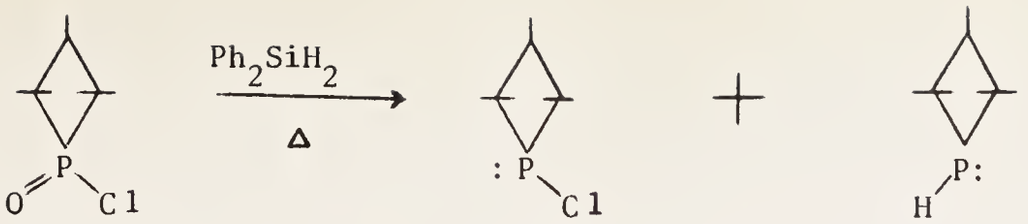


(5) (47) (48)

Following the method of Griffin [36], the acid chloride (5) was heated with phosphorus pentasulfide to obtain a mixture of isomeric thioacid chlorides (47). The latter was reduced to the chlorophosphetane (48) with tri-(n-butyl) phosphine [37]. This reaction is an equilibrium process and the product must be removed as it is formed in order to drive the equilibrium to the right [36]:

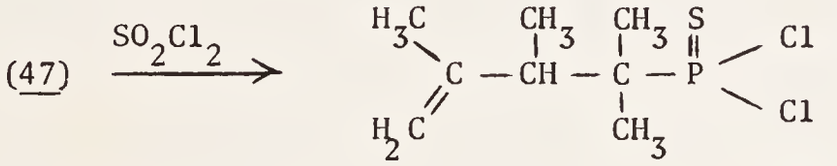
$$R_3P = S + (nBu)_3P: \rightleftharpoons R_3P: + (nBu)_3P=S$$

the chlorophosphetane (48)(cis:trans::1:2) was distilled by passing a current of dry nitrogen gas through the reaction mixture. Trippett [36] has recently reported the synthesis of (48) by another route. This was accomplished by the reduction of (5) with diphenylsilane to yield a mixture of products in an unspecified yield:



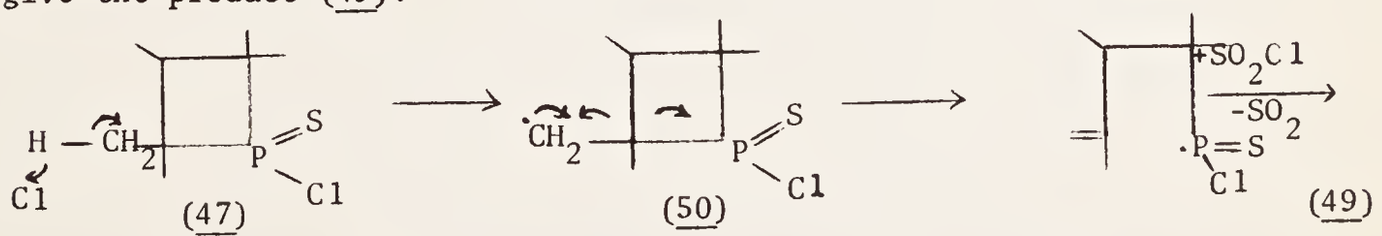
(48)

In an attempt to convert the thioacid chloride (47) to a mixture of isomeric acid chlorides (5) with sulfuryl chloride [39], an unexpected product was obtained (49). The ring open product was characterized by its ir, nmr, and elemental analysis.

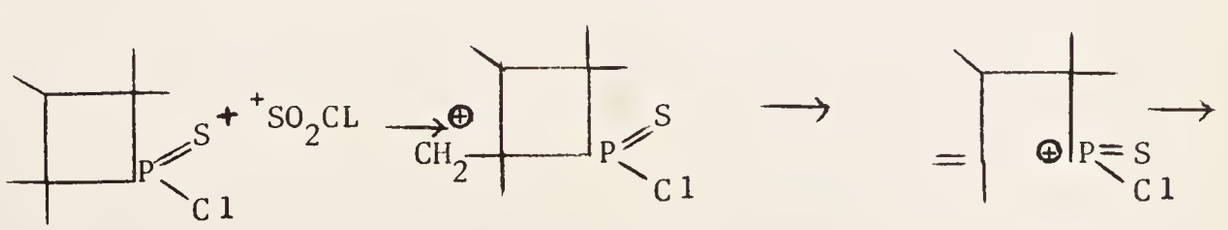


(49)

The formation of (49) can be visualized to have occurred by either a radical or a polar mechanism. In the radical [40] mechanism, a chlorine atom could abstract an atom of hydrogen from one of the α-methyl groups. The resulting radical (50) would undergo ring-opening to yield the phosphorus radical (51) which would subsequently abstract a chlorine atom to give the product (49):



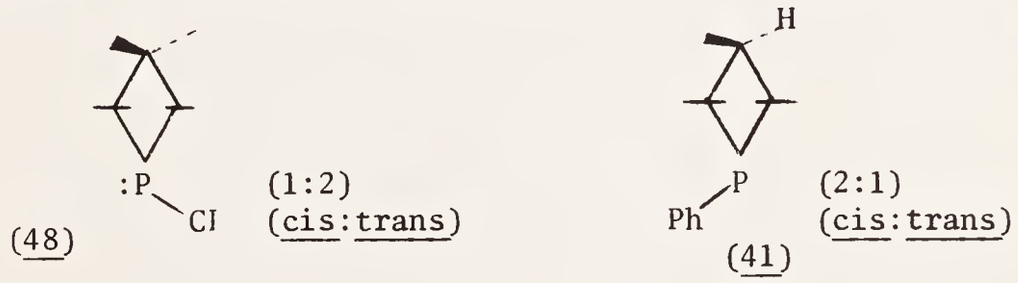
The polar mechanism [41] would involve an attack by $(SO_2Cl)^+$ ion as shown below:



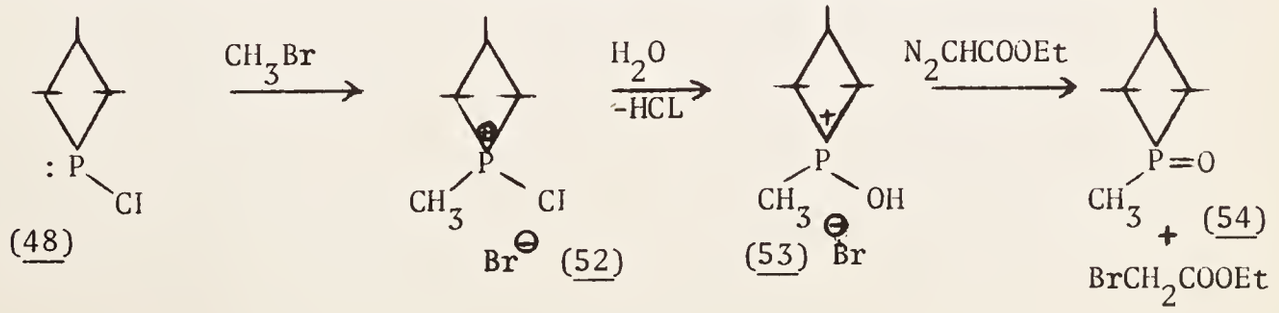
(49)

An attack at the sulfur atom of the thioacid chloride may also be envisioned, which is in keeping with the fact that the acid chloride (5) does not react with sulfuryl chloride.

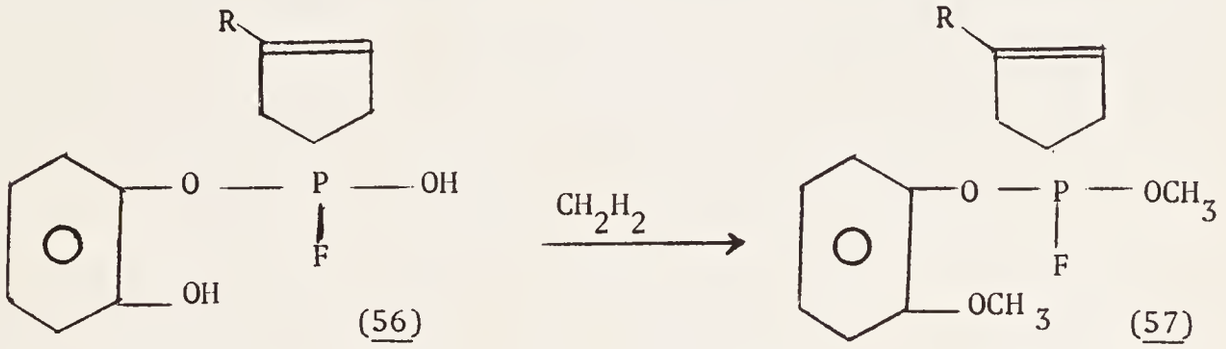
As pointed out earlier, the chlorophosphetane (48) was obtained as a mixture of isomers in which the predominant isomer was trans. The assignment was based on ^{1}H and ^{31}p nmr data. Treatment of a 1:2 (cis : trans) mixture of (48) with phenyllithium gave a 2:1 (cis : trans) mixture of phenylphosphetane (41). This conclusively shows that nucleophilic substitution at phosphorus in this compound proceeded with inversion of configuration:

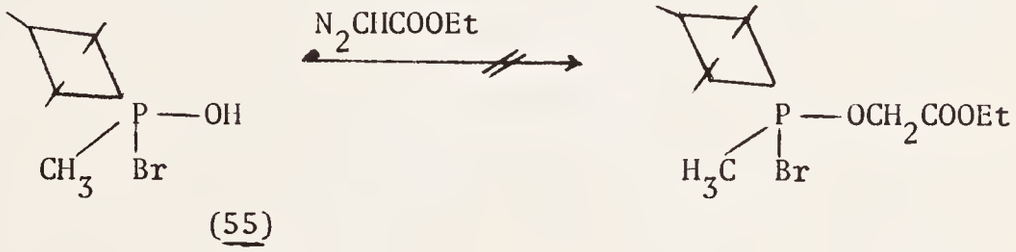


Similar conclusions have been reported by Trippett [38]. Quaternization of the phosphetane (48) would be expected to yield a salt analogous to the intermediate (4) formed during the cyclization reaction (p. 3). Treatment of (48) with methyl bromide followed by recrystallization from acetonitrile gave a compound which showed the absence of chlorine in the elemental analysis. The product gave a satisfactory analysis for a compound in which the chloro substituent had been replaced by a hydroxyl group. In order to verify the proposed structure (53), the compound was treated with ethyldiazoacetate. The products of the reaction were identified as ethyl bromoacetate (by glpc) and 1,2,2,3,4,4-hexamethylphosphetane oxide (54).



The addition of the elements of hydrobromic acid to ethyl diazoacetate supports the structure (53), although a pentacovalent structure (55) cannot be completely ruled out. Recently, Petrov and co-workers [42] have demonstrated that a hydroxyphosphorane (56) could be converted to the corresponding methoxyphosphorane (57) by treatment with diazomethane:





By consideration of this analogy, it may be argued that if the compound had structure (55), the corresponding alkoxy compound would have been formed on treatment with ethyl diazoacetate. However, it should be emphasized that little is known about hydroxyphosphonium salts (58) or hydroxyphosphoranes (59) and the analogy drawn here may not be valid.

In any event, the stage at which incorporation of the hydroxy group occurs is not clear. It is likely that it occurred either during the work-up or through the moisture in the solvent during quaternization (ether) or re-crystallization.

3. Experimental

Nuclear magnetic resonance spectra were recorded on a Varian Associates Model A-60 spectrometer with tetramethylsilane as an internal standard. The ^{31}P-^{1}H decoupling experiments were performed on an NMR Specialties Model HD-60A heteronuclear spin decoupler in conjunction with A-60 spectrometer. The infrared spectra were recorded on Perkin-Elmer Model 21 and 237 spectrophotometers. Microanalyses were performed by Alfred Bernhardt, Microanalytisches Laboratorium, Mulheim (Ruhr), West Germany. All boiling points and melting points (Thomas-Hoover apparatus) are uncorrected. Solvents during the reaction work-up were removed with a rotating evaporator. Reactions involving trivalent phosphorus compounds were conducted and processed under an atmosphere of nitrogen.

Synthesis of 1-Chloro-2,2,3,3,4-penatmethylphosphetane 1-Oxide (7); To a mixture of 13.15 (0.1 mole) of anhydrous aluminium chloride and 13.75 (0.1 mole) of phosphorus trichloride in 95 ml of methylene chloride in a 3-necked round bottomed flask equipped with a mechanical stirrer, an addition funnel, a thermometer, a nitrogen inlet and an anhydrous calcium chloride guard-tube, was added 11.2g (0.1 mole) of 3,4,4-trimethyl-2-pentene in 10ml of methylene chloride at 0-5 °c with stirring over 90 min.. The mixture was stirred overnight and then quenched by pouring over 200g of ice with stirring. The two layers were separated, the aqueous layer was extracted with methylene chloride, and the combined organic layers were

washed with ice-cold water. The organic layer was dried over anhydrous sodium sulfate and evaporated to give 18.5 g brown semi-solid. Recrystallization from benzene-petroleum ether (30-60°) gave 9.8g (50%) of white crystalline solid, m.p. 114-119°. The nmr ($DCCl_3$) showed peaks at τ=8.54 (3H, d, $^3J_{PCCH}$=22 cps), τ=8.72 (3H, d, $^3J_{PCCH}$=22 cps), τ=8.77(3H, 2d, ^{3}PCCH= 23.5 cps, $^3J_{HCCH}$=7.5 cps), τ=6.79 (1H,2q, $^2J_{PCH}$=14.5 cps, $^2J_{HCH}$=7.0 cps), τ=8.92 (6H,s).

Synthesis of 1-Hydroxy-2,2,3,3,4-pentamethylphosphetane 1-Oxide (9) from (7). A mixture of 1.0g (0.0051 mole) of acid chloride (7) and 10ml of 1M sodium hydroxide solution was stirred overnight. The resulting mixture was extracted twice with benzene and then the aqueous layer was acidified with concentrated HCl. The solution was extracted with methylene chloride and the organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave 0.8g pale yellow oil which solidified on cooling, m.p. 103-104.5°. The nmr ($DCCl_3$) exhibited peaks at τ=8.94 (3H, 2d, $^3J_{PCCH}$=21.5 cps, $^3J_{HCCH}$=7.0 cps), τ=8.91 (3H,d, $^3J_{PCCH}$= 19.5 cps), τ=8.78 (3Hd, $^3J_{PCCH}$=19.0 cps), τ=8.99 (6H,s), τ=7.0-7.7 (1H, ring, m), τ=1.19 (1H,s).

The compound was sublimed three times in vacuo at 100° (0.05mm) to obtain the analytical sample, a white powder, m.p. 104-104.5°.

Anal. Calcd. for $C_8H_{17}O_2P$: C, 54.53; H,9.72; Found: C, 54.29; H, 9.60.

Synthesis of 1-Methoxy-2,2,3,3,4-pentamethylphosphetane 1-Oxide (8) from (7). A solution containing 0.1 mole of sodium methoxide was prepared from 2.3g (0.1g atom) sodium metal in 100 ml absolute methanol. To this stirred solution at room temperature was added a solution of 19.5g (0.1 mole)

of acid chloride (7) in 100 ml methanol over 1 hr.. The temperature of the reaction mixture was maintained near 20° with an ice-water bath. The mixture was stirred overnight, the solvent evaporated, and the residue was washed with 400 ml methylene chloride in portions and filtered. Evaporation of the filtrate gave 23.0g crude liquid. A bulb to bulb distillation in vacuo (30-40° at 0.2 mm) gave 18.5g liquid that solidified on standing. The hygroscopic compound was recrystallized from petroleum ether (30-60°) to give a crystalline solid m.p. 105-107°. The nmr (benzene) showed peaks at: τ = 6.39 (3H, d, $^3J_{POCH}$=10.0 cps), τ=9.06 (3H, d, $^3J_{PCCH}$=19.6 cps), τ=8.80 (3H, d, $^3J_{PCCH}$=19.5 cps), τ=8.91 (3H, 2d, $^3J_{PCCH}$=21.5 cps. $^3J_{HCCH}$=7.5 cps), τ = 9.21 (6H,s), τ=7.37 (1H, 2q, $^2J_{PCH}$=14.5 cps, $^2J_{HCH}$=7.0 cps).

Synthesis of 1-Chloro-2,2,3,4-tetramethylphosphetane 1-Oxide (10). To a mixture of 13.15g (0.1 mole) anhydrous aluminum chloride and 13.75g (0.1 mole) phosphorus trichloride in 95 ml of methylene chloride in a 3-necked round bottom flask equipped with mechanical stirrer, an addition funnel, a thermometer, a nitrogen inlet and an anhydrous calcium chloride guard-tube, was added 9.8g (0.1 mole) 4,4-dimethyl-2-pentene in 10 ml of methylene chloride at 0-5° with stirring over 105 min. . The mixture was stirred overnight at room temperature and then quenched by pouring over 200 g of ice with stirring. The two layers were separated, the aqueous layer extracted with methylene chloride, and the organic layers were dried over anhydrous sodium sulfate, and then evaporated to give 17.5g solid. Recrystillization from petroleum ether (30-60°) gave a white crystalline solid m.p. 99-103°, 20.5-24.0g (56-66%). The nmr (benzene) showed peaks at τ=7.52 (2H, m), τ=8.95 (3H, d, J=22.0 cps), τ=9.00 (3H, d, J_{PCCH}=23.5 cps), τ=9.25 (3H, 2d, $^3J_{PCCH}$=14.0 cps), $^3J_{HCCH}$=7.0 cps), τ=9.44 (3H, d, $^3J_{HCCH}$=7.0 cps).

Synthesis of 1-Methoxy-2,2,3,4-tetamethylphosphetane 1-Oxide (11). A solution of 0.1 mole of sodium methoxide was prepared by dissolving 2.3g (0.1g atom) of sodium metal in absolute methanol. To this stirred solution was added a solution of 18.05g of acid chloride (10) in 100 ml of methanol at room temperature for 1 hr.. The temperature of the exothermic reaction was maintained near 20° with an ice-water bath. A white precipiate formed during the addition. The mixture was stirred overnight, the solvent evaporated and the residue was washed with 400 ml of methylene chloride, in portions and filtered. Evaporation of the solvent from the filtrate gave 18.5g crude viscous liquid. Distillation in vacuo gave a clear liquid b.p. 62.0-62.5° (0.1 mm) which solidified on cooling (85%). The nmr (benzene) showed the liquid to be a single isomer with peaks at τ=6.42 (3H, d, $^{3}J_{PCCH}$=10.0 cps), τ=7.30-8.00 (2H, m), τ=8.98 (3H, d, $^{3}J_{PCCH}$=19.0 cps), τ=9.05 (3H, d, $^{3}J_{PCCH}$=18.5 cps), τ=8.99 (3H, 2d, $^{3}J_{PCCH}$= 20.0 cps), $^{3}J_{HCCH}$=7.0 cps), τ=9.25 (3H, broad d, $^{3}J_{HCCH}$=6.5 cps).

Synthesis of 1-Hydroxy-2,2,3,4-tetramethylphosphetane 1-Oxide (12). To 1.0g of acid chloride (10) was added 10 ml of 10% sodium hydroxide solution and the mixture was stirred overnight. The resultant mixture was extracted with benzene and then the aqueous layer was acidified with concentrated HCl The solution was extracted with methylene chloride, the combined organic layers were washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave 0.82g of oil that solidified on standing. Recrystallization from hexane gave 0.75g of white powder-like solid m.p. 71-74° (94%). The nmr ($DCCl_3$) showed peaks at: τ =8.78 (3H, d, $^{3}J_{PCCH}$= 19.5 cps, τ =8.85 (3H, d, $^{3}J_{PCCH}$=19.0 cps), τ =8.80 (3H, 2d, $^{3}J_{PCCH}$=20.0 cps, $^{3}J_{PCCH}$=7.0 cps), τ =9.0 (d, $^{3}J_{HCCH}$=7.0 cps), τ =7.30-8.00 (1H, m), τ =1.76 (1H, s). Anal. calcd. for: $C_7H_{14}O_2P$: C,52 17, H, 8-76. Found: C,5196; H, 8.90.

Synthesis of 1-Methoxy-2,2,3,3-tetramethylphosphetane 1-Oxide (15). To a mixture of 66.7g (0.5 mole) of anhydrous aluminum chloride and 68.78g (0.50 mole) of phosphorus trichloride in 200 ml of methylene chloride at 0-5° was added with stirring, 49.0g (0.5 mole) of 2,3,3-trimethyl-1-butene in 200 ml of methylene chloride over 3 hr. under anhydrous conditions. The mixture was stirred overnight and then the reaction was quenched by pouring it over 400g of ice. The two layers were separated, the aqueous layer extracted with methylene chloride and the combined extracts were dried over anhydrous sodium sulfate. Evaporation of the solvent gave 83g of crude viscous liquid.

To the stirred solution of 83g of the above crude liquid in 325 ml of anhydrous benzene was added 45.2g (0.45 mole) of trieth lamine followed by 15.3g (0.5 mole) of methanol in 125 ml of benzene over 1 hr.. After the exothermic reaction ceased, the mixture was allowed to reflux for 2 hr.. A crystalline precipitate formed which was filtered, and washed with benzene. Evaporation of the solvent gave a pale brown liquid which turned to a semi-solid on standing. A bulb to bulb distillation (25-30° at 0.1 mm) gave 40.1g of plates m.p. 50-52° (23%) over all. The nmr (benzene) showed peaks at τ=6.45 (3H, d, $^{3}J_{POCH}$-11.0 cps), τ= 9.00 (3H, d, $^{3}J_{PCCH}$=19.0 cps), τ= 8.88 (3H, d, $^{3}J_{PCCH}$=15.5 cps), τ=9.05 (3H,s), τ=9.03 (3H,s), τ=7.81 (1H, d, $^{2}J_{PCCH}$=15.5 cps), τ=7.90 (1H, d, $^{2}J_{PCH}$=14.5 cps).

Compound (15) was recrystallized from petroleum ether (30-60°) and sublimed in vacuo at 25-30° (0.2-0.4 mm) to obtain plates, m.p. 52-55°. Anal. Calc. for $C_8H_{17}O_2P$: C,54.53; H,9.73; P, 17.58. Found: C, 54.59; H,10.02; P,17.56.

Prepatation of 1-Hydroxy-2,2,3,3-tetramethylphosphetane 1-Oxide (13). A mixture of 1.0g (0.57 mole) of the ester (15) and 10 ml of 10% sodium hy-

droxide was stirred overnight. Washing the solution with benzene followed by acidification with concentrated HCl gave an oil which was extracted with methylene chloride. The organic layer was washed with water and heated over anhydrous sodium sulfate. Evaporation of the solvent gave 0.92 (100% of solid, m.p. 175-183°) The nmr ($DCCl_3$) exhibited peaks at: τ=8.83 (6H, d, $^3J_{PCCH}$=20.0 cps), τ=8.88 (6H, 2s), τ=7.61 (2H, d, $^2J_{PCH}$=15.5 cps).

Preparation of 1-Chloro-2,2,3,3-tetramethylphosphetane 1-Oxide (14). To 14.1g (0.087 mole) of the acid (13) was added 11.9g (0.1 mole) of thionyl chloride. The resulting mixture was heated to reflux for 4 hr.. The excess of thionyl chloride was evaporated and the residue was distilled in vacuo at 66° (0.2 mm) to give 12.1g (77%) of the acid chloride (14). The nmr (benzene) showed peaks at τ=8.75 (3H, d, $^3J_{PCH}$=20 cps), τ= 8.85 (3H, d, $^3J_{PCCH}$=25 cps), τ= 8.92 (6H, broad s,), and τ=7.27 (2H, d, $^2J_{PCH}$= 16.0 cps) (*).

Preparation of 1-Phenyl-2,2,3,4-tetramethylphosphetane 1-Oxide (16). To a homogenous solution prepared from 35.8g (0.2 mole) of phenylphosphonous dichloride and 26.7g (0.2 mole) of anhydrous aluminum chloride in 280 ml of methylene chloride at 0-5°, was added 19.6g (0.2 mole) of 4,4-dimethyl-2-pentene in 60 ml of methylene chloride over 2 hr. with stirring and under anhydrous conditions. The mixture was stirred overnight and the reaction was quenched by adding 200 ml of ice-water dropwise to the stirred mixture of 0-5° over 2 hr.. The two layers were separated, the aqueous layer extracted with methylene chloride and the combined extracts were washed with water and dried over anhydrous sodium sulfate. Evaporation gave 47.1g of a

(*) This peak is an apparent doublet but is probably a more complex J_{ABX} system.

crude viscous liquid. Distillation of the liquid in vacuo gave 10.0g liquid, b.p. 110° (0.2-0.4 mm) which solidified on cooling (22.4%). The nmr (CCl_4) showed one isomer with peaks at: τ=1.9-2.6 (5H,m), τ=9.14 (3H, d, $^3J_{PCCH}$=19.0 cps), τ=8.71 (3H, d, $^3J_{PCCH}$=17.0 cps), τ= 8.70 (3H, 2d, $^3J_{PCCH}$=18.5 cps, $^3J_{HCCH}$=7.5 cps), τ=8.90 (3H, 2d, $^4J_{PCCCH}$=1 cps, $^3J_{HCCH}$= 7.0 cps), τ=6.30-7.20 (1H,m), τ= 7.30-8.10 (1H,m)

Synthesis of 1-Phenyl-2,2,3,4-tetramethylphosphetane (17).A complex of 4.9g (0.062 mole) pyridine and 8.7g (0.065 mole) trichlorosilane in 50 ml benzene at 0-5° was prepared under anhydrous conditions and under a flow of nitrogen. To this mixture was added with stirring, 4.5g (0.02 m) of the phosphine oxide (16) in 60 ml of benzene at 0-5° for 2 hr.. The cold bath was removed and the mixture was allowed to reflux for 3.5 hr.. The mixture was stirred overnight and then quenched by adding 100 ml of 20% sodium hydroxide solution dropwise at 0.5° until two clear layers were obtained. The aqueous layer was separated, extracted with benzene and the combined layers were washed with water and saturated sodium chloride solution. Drying of the organic layer over sodium sulfate followed by evaporation gave 2.5g (60%) of a liquid with a characteristic phosphine odor.

Preparation of 1-Methyl-1phenyl-2,2,3,4-tetramethylphosphetanium Iodide (18). The above liquid was dissolved in 20 ml of anhydrous ether and treated with 5 ml of methyl iodide and allowed to stand overnight. The precipitate was filtered, washed with ether and then immediately recrystallized from acetonitrile-ether acetate to give 2.30g of pale yellow needles m.p. 209-213° (decomposition) (32% over all). The nmr ($DCCl_3$) showed peaks at: τ=7.35 (3H, d, $^2J_{PCCH}$=13.5 cps), τ=8.37 (3H, d, $^3J_{PCCH}$=21.0 cps), τ= 8.74 (3H, d, $^3J_{PCCH}$=21.0 cps), τ=8.81 (3H, 2d, $^3J_{HCCH}$=7.0 cps, $^4J_{PCCH}$= 1.0 cps) τ=8.44 (3H 2d, $^3J_{PCCH}$=22.0 cps, $^3J_{HCCH}$=7.0 cps), τ=5.50-6.25 (1H, m), τ=6.50-7.30 (1H, m), τ=1.50-2.50 (5H, aromatic).

Anal. calcd. for $C_{14}H_{22}IP$: C, 48.29; H, 6.37; I, 36.45. Found: C, 48.36; H, 6.51; I, 36.45. Found: C, 48.56, H, 6.31.

Preparation of 1-Methylene-2,2-dimethylcyclohexane. To 184g (0.515 mole) of triphenylmethylphosphonium bromide suspended in 1.1 of ether was added 400 ml of 1.3 M n-butyllithium in pentane solution at 0°. The orange colored solution was stirred for several hours at room temperature.

To the above solution at 0° under nitrogen was added 50g (0.397 mole) of 2,2-dimethylcyclohexanone in 200 ml of ether over 4 hr. with stirring. A precipitate formed with the contact of the two solutions. The stirring of the reaction mixture became more difficult as the reaction progressed and so the mixture was allowed to stand overnight. The reaction was quenched by pouring the mixture over ice and the precipitated solid was filtered. The filtrate was separated, and the ether layer was dried over anhydrous sodium sulfate. Evaporation of the ether followed by distillation of the crude liquid in a spinning band column gave 20g liquid at 139-142° at atmospheric pressure. (40%). The ir of neat liquid showed a strong absorption at 1640 cm^{-1}. The nmr (neat) showed peaks at: τ=5.38 (2H, s, vinyl), τ=7.82 (2H, m, allyl), τ=8.52 (6H, m, alkyl), τ=8.98 (6H, s, methyl).

Preparation of 1,6-Dimethyl-7-phenyl-7-phosphabicyclo-(4,2,0)-octane 1-Oxide. To a homogenous solution of 25g (0.14 mole) of phenylphosphorous dichloride and 20g (0.15 moel) of anhydrous aluminum chloride in 500 ml of methylene chloride was added a solution of 19g (0.153 mole) of the above alkene in 500 ml of methylene chloride at 0° over 4 hr. with stirring. The mixture was poured over ice, the layers were separated and the methylene chloride layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a viscous liquid which was distilled b.p. 155-160° (0.1 mm) to obtain 10.6g (28%) of a colorless liquid.

Preparation of 1,6,7-Trimethyl-7-phenyl-7-phosphonia-bicycle(4,2,0)-octane Bromide (19). To a stirred solution of 10.0g (0.04 mole) of the phosphine oxide described above in 300 ml of benzene under nitrogen, was added 5.1g (0.05 mole) of triethylamine followed by 6.9g (0.05 mole) of trichlorosilane. The nixture was heated to reflux for 15 hr., cooled and quenched by adding 80 ml of 20% sodium hydroxide solution dropwise with stirring. The layers were separated, and the benzene layer was washed well with saturated sodium chloride solution and dried over anhydrous sodium sulfate. The solvent was evaporated and the resulting material was dissolved in benzene-ether, and treated with excess of methyl bromide in a pressure flask for 2 days. The resulting glassy solid was recrystallized from acetonitrile-ethyl acetate to give 3.0g of a solid, m.p. 191-194°. The nmr ($DCCl_3$) showed the compound to be a single isomer having peaks at: τ=1.25-2.60 (5H, m, aromatic), τ=6.60 (2H , 2d, J_{PCH}=13.5 cps, J_{HCH}=3.0 cps), τ=7.20 (3H, d, $^2J_{PCH}$=14.0 cps), τ=8.0-9.0 (14 H, broad absorption).

The compound (19) was recrystallized several times for the analytical sample m.p. 192-195°. Anal. calcd. for $C_{16}H_{24}PBr$: C,58.71; H, 7.39, P,9.39; Br, 24.48. The compound has been submitted to Prof. Trefonas for X-rays investigation.

Preparation of 1-Benzyl-2,2,3,4,4-pentamethylphosphetane 1-Oxide (25). A Gringnard reagent was prepared from 25.2g (0.224 mole) of benzyl chloride and 4.75g (0.2g atom) of magnesium turnings in 150 ml of anhydrous ether.

The above Grignard reagent was added to 38.9g (0.2 mole) of acid chloride (5) in 500 ml of ether at 0-5° with stirring over 2 hr.. The mixture was stirred for an additional one half hr. and then the reaction was quenched with a saturated solution of ammonium chloride. A white solid separated which was dissolved by adding an excess of ether. The organic layer was se-

parated, washed with 5% sodium bicarbonate and then dried over anhydrous sodium sulfate. The ether solution on evaporation gave a white solid which was recrystallized from cyclohexane to obtain 30g of a crystalline solid, m.p. 187-188° (60%). The nmr ($DCCl_3$) showed peaks at: τ=2.40-2.92 (5H, m, aromatic), τ=6.75 (2H, d, $^2J_{PCH}$=10.5 cps), τ=8.78 (6H, d, $^3J_{PCCH}$= 15.5 cps), τ=8.85 (6H, d, $^3J_{PCCH}$=17.5 cps), τ=9.12 (3H, dd, $^4J_{PCCCH}$= 1.8 cps, $^3J_{HCCH}$=7.5 cps), τ=8.02-8.50 (1H, m, $^3J_{PCCH}$=7.5 cps). Anal. calcd. for $C_{15}H_{23}OP$: C, 72.00; H, 9.20. Found: C, 72.16; H, 9.08.

Reduction and Quaternization of (25); Preparation of 1-Benzyl-1,2,2, 3,4,4-hexamethylphosphetanium Bromide (24). To a complex prepared from 4.05g (0.03 mole) of trichlorosilane and 3.5g (0.035 mole) of triethylamine in 90 ml of benzene was added a solution of 7.5g (0.03 mole) of the oxide (25) in 120 ml of benzene over 10 min. at 0-5° with stirring under an atmosphere of nitrogen. The cold bath was removed and the mixture was allowed to reflux for 3 hr.. The reaction was quenched by adding a 20% sodium hydroxide solution at 0-5° until two clear layers were obtained. The organic layer was separated, the aqueous layer was extracted with benzene and the combined benzene layers were washed with saturated sodium chloride solution and then dried over anhydrous sodium sulfate. Evaporation of the solvent gave a white solid which was dissolved in 20 ml of ether and then treated with 5 ml of methyl bromide in a sealed flask for 24 hr.. The precipitated solid was filtered and recrystallized from acetonitrile to obtain 7.2g of needles, m.p. 207-214° (80%). Repeated recrystallization raised the m.p. to 213-218°. The nmr ($DCCl_3$) showed peaks at: τ=2.23-2.97 (5H, m, aromatic), τ=5.23 (2H, d, $^2J_{PCH}$=14.5 cps), τ=6.75-7.25 (1H, m), τ=7.82 (3H, d, $^2J_{PCH}$= 13.5 cps), τ=8.31 (6H, d, $^3J_{PCCH}$=18.5 cps), τ=8.60 (6H, d, $^3J_{PCCH}$19.5 cps), τ=8.98 (3H, dd, $^3J_{HCCH}$=7.0 cps, $^4J_{PCCCH}$=1 cps).

Preparation of the Dibenzyl Salt (26). The phosphine was prepared as described above and then treated with 5 ml of benzyl bromide and the mixture was allowed to stand in a sealed flask for 4 days. The precipitate was filtered, washed with ether and then recrystallized from acetonitrile to give 6.3g of crystalline needles m.p. 219.5-222.50. (50%). The nmr CF_3COOH) showed peaks approximately at: τ=2.70-3.50 (10H, m, aromatic), τ=6.30 (4H, 2d, each $^2J_{PCH}$=12.5 cps), τ=8.60 (6H, d, $^3J_{PCCH}$=19.3 cps), τ=8.65 (6H, d, $^3J_{PCCH}$=19.8 cps), τ=9.08 (3H, dd, $^3J_{HCCH}$=7.0 cps), $^4J_{PCCCH}$=1 cps). Anal. calcd. for $C_{22}H_{30}BrP$: Br, 19.71. Found: Br, 19.66,19.85.

Preparation of 1-(1-Naphthyl)-2,2,3,4,4-pentamethylphosphetane 1-Oxide. A Grignard reagent was prepared from 25g (0.1 mole) of 1-iodonaphthalene and 2.5g (0.1 g. atom) of magnesium turnings in 200 ml of ether. This solution was added to a solution of 22g (0.11 mole) of the acid chloride (5) in 300 ml of ether with stirring in a three-necked flask under nitrogen at 0° over 40 min.. The reaction was allowed to start at room temperature for 6 hr.. A viscous oil formed at the bottom of the mixture. The reaction was quenched with a saturated solution of ammonium chloride at 0°. An insoluble precipitate was formed which was filtered and recrystallized from ethanol-water and subsequently from cyclohexane to give 3.5g (11.2%) of the product m.p. 177-181°.

The ether layer was evaporated and the residue was treated with petroleum ether (30-60%). The ppt. was collected, recrystallized and sublimed to give 0.6g of additional product m.p. 179-182°. The nmr ($DCCl_3$) showed peaks at: τ=1.55-2.68 (7H, m), τ=7.40 (1H, 6, $^3J_{HCCH}$=7.0 cps, $^3J_{PCCH}$=3.0 cps), τ=9.01 (3H, 2d, $^3J_{HCCH}$=7.0 cps, $^4J_{PCCCH}$=1.2 cps), τ=8.40 (6H, d, $^3J_{PCCH}$=16.5 cps), τ=8.75 (6H, d, $^3J_{PCCH}$=18.0 cps). Anal. calcd. for $C_{18}H_{23}OP$: C,75.49; H,8.10. Found: C, 75.45; H, 8.17.

Preparation of 1-(1-Naphthyl)-1,2,2,3,4,4-hexamethylphosphetanium Bromide (31). To a solution of 8.3g. (0.029 mole) of the above phosphetane oxide in 170 ml of benzene was added 3.2g (0.032 mole) of triethylamine followed by 4.5g (0.032 mole) of trichlorosilane. The mixture was heated to reflux for 2 hr. under nitrogen atmosphere, cooled and treated with 20% sodium hydroxide solution until distinct layers were obtained. The two layers were separated, the organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated to give the phosphine which was dissolved in ether and treated with an excess of methyl bromide in a sealed flask. After standing for several days, the product was filtered to give 10.3g solid m.p. 248-254°. The nmr (trifluoroacetic acid) showed the salt to be a mixture of isomers with peaks at: τ=9.00 (3H, 2d, $^{3}J_{HCCH}$=7.0 cps $^{4}J_{PCCCH}$=1.3 cps), τ=7.74 (3H, d, $^{2}J_{PCH}$=13.0 cps), τ=7.10 (1H, 0, $^{3}J_{PCCH}$=2.0 cps, $^{3}J_{HCCH}$=7.0 cps), τ=8.42 (6H, d, $^{3}J_{PCCH}$=20.5 cps), τ=8.60 (6H, d, $^{3}J_{PCCH}$=19.0 cps), τ=1.70-2.80 (7H, m, aromatic).

The product was recrystallized from acetonitrile-ethyl acetate to give the analytical sample. Anal. calcd. for $C_{19}H_{26}P$ Br: C, 62.47; H, 7.17. Found: C, 62.44; H, 7.42.

Alkaline Decomposition of the Salt (31). A solution of 3.8g (0.01 mole) of the salt (31) was treated with 1.0g of sodium hydroxide in 3 ml of water at 0° with stirring. The product was extracted in benzene and the benzene solution was washed with water, dried over anhydrous sodium sulfate and was evaporated to a viscous oil. The nmr ($DCCl_3$) exhibited peaks at: τ=6.50-6.90 (2H, m, allyl), τ=3.70-4.70 (2H, m, vinyl), τ=8.20 (1H, m), τ=8.62 (3H, d, $^{3}J_{PCCH}$=12.0 cps), τ=8.72 (3H, d, $^{3}J_{PCCH}$=14.0 cps), τ=8.74 (3H, d, $^{3}J_{PCCH}$=15.0 cps), τ=8.89 (3H, s), τ=9.30 (3H, s).

The product from the above reaction was dissolved in 150 ml of decalin

and heated with 1g of 30% palladium on charcoal at reflux for 4 days, while a stream of nitrogen was bubbled through the reaction mixture. The mixture was cooled, filtered, and evaporated (40°, 0.1 mm) to give a solid residue (1.2g). Recrystallization of the product from cyclohexane gave 900 mg. of the pure compound m.p. 173-176°. The ir (nujol mull) of the product showed a strong absorption at 1150 cm^{-1}. The nmr ($DCCl_3$) showed peaks at: τ=2.00 -2.70 (6H, m, aromatic), τ=8.28 (3H, d, $^2J_{PCH}$=12.0 cps), τ=8.91 (3H, d, $^3J_{HCCH}$=7.0 cps), τ=8.60 (3H, s), τ=8.72 (3H, s), τ=8.78 (3H, d, $^3J_{PCCH}$= 14.0 cps), τ=8.72 (3H, d, $^3J_{PCCH}$=15.0 cps). Anal. calcd. for: $C_{19}H_{25}OP$: C, 75.96; H, 8.39; P, 10.31. Found: C, 75.83; H, 8.52; P, 10.42.

Synthesis of precursors for (34).

Preparation of 2-Phenyl-2-bromocinnamic-Acid. In a 500 ml three-necked round bottomed flask equipped with a condenser, a mixture of 80.g (0.43 mole) of o-bromobenzldehyde, 58.8g (0.43 mole) of phenylacetic acid, 43.6g (0.43 mole) of triethylamine and 64.7g (0.63 mole) of acetic anhydride was refluxed for 3 hr. (temperature of the mixture 164-165°). A fresh 10 ml portion of triethylamine was added and the mixture was allowed to reflux for an additional hour. The reaction was cooled and the resulting brown viscous liquid was dissolved in 500 ml of benzene. The benzene solution was slowly treated with 20% sodium hydroxide solution in a separatory funnel. On shaking the latter, three layers were formed. The thick bottom layer was the solution of the salt of the desired product. Separation, acidification with 6M HCl, with cooling, gave a precipitate which was dissolved in benzene. The benzene solution was washed with water, dried over anhydrous sodium sulfate and evaporated to give a solid. Recrystallization of the solid from ethyl acetate (using Norit) gave 100g of crystalline solid m.p. 178-182°.

Preparation of 1-Bromostibene. A mixture of 50g (0.166 mole) of 2-phenyl-2-bromocinnamic acid, 244 ml of quinoline and 4.0g of copper chromite catalyst was heated in a round bottomed flask with a condenser to 2100-225° and maintained at that temperature for 80 min. during which evolution of carbon dioxide occurred. After the evolution of the gas had ceased, the mixture was cooled. Removal of quinoline in vacuo gave 48.7g of a dark brown liquid. Distillation of the liquid residue gave a pale yellow liquid, b.p. 130-135° (0.6-0.7 mm) (29.0g). The product was dissolved in 75 ml of ether, washed with 10% HCl followed by saturated sodium bicarbonate solution.

The ether solution was dried over anhydrous sodium sulfate. Distillation of the product gave 19.5g of the pale yellow liquid, b.p. 115-118° (0.2-0.3 mm) (44%).

Preparation of 1-Bromophenanthrene. In a quartz flask with cooled copper tubing inside for cooling, was placed 3-5g of the above 1-bromostilbene and 100-200 mg iodine in 2 l of cyclohexane. The solution was irradiated using Hanovia lamp (450 watts) surrounded by a corex filter. The temperature of the solution was maintained between 25-30°. The progress of the reaction was followed by taking aliquots and observing the disappearance of 960 cm^{-1} peak of stilbene in the ir. After the peak diminished (34-36 hr.), a fresh portion of the stilbene and iodine was added and the process continued until a total of 19.5g of stibene had been added. Evaporation of the solvent gave a crude semi-solid. Recrystallization of the product from ethanol yeilded 7.55g 1-bromophenathrene, m.p. 105-108° Recrystallization from acetonitrile raised the m.p. to 110-112°. (109.5 - 110°) (43).

Preparation of 1-(1-Phenanthryl)-2,2,3,4,4-pentamethylphosphetane 1-Oxide (34). A solution of 5.9g (0.023 mole) of 1-bromophenanthrene in 30 ml of warm benzene was added dropwise to 0.32g (0.046g atom) of cut lithium wire in 40 ml of anhyd ether. The mixture which gradually turned deep brown in color was allowed to reflux for 3 hr. and then allowed to stand for 5 hr. at room temperature. A test with Gilman's reagent was positive.

The above organolithium compound was added to 10.5g (0.054 mole) of the acid chloride (5) in 250 ml of ether with stirring at -40° over 15 min. The mixture was stirred at room temperature overnight and then quenched with a saturated solution of ammonium chloride. An insoluble precipitate was formed which was filtered and recrystallized from ethanol to yield 0.89g of a solid, m.p. 195-205°. The ether-benzene filtrate was stirred with 100 ml of 10% sodium hydroxide solution (to remove any unreacted acid chloride) and subsequently washed with water, dried and evaporated to give 0.40g of additional product, m.p. 201-204°. The ir (1160 and 1178 cm^{-1}, P[O]) of each of the products was identical. The compound was sublimed at 150° (0.1 mm) and recrystallized from ethanol-water and cyclohexane to give flat, silvery needles, m.p. 202-204°. The nmr ($DCCl_3$) showed peaks due to the major isomer at: τ=1.50-2.70(9H, m, aromatic), τ=8.43 (6H, d, $^3J_{PCCH}$=16.0 cps), τ=8.72 (6H, d, $^3J_{PCCH}$=17.0 cps), τ=8.90 (3H, 2d, $^3J_{HCCH}$=7.0 cps , $^4J_{PCCCH}$= 1.8 cps), τ=8.10 (1H, m). Anal. Calcd. for $C_{22}H_{25}OP$: C,7854; H, 7.49; P, 9.21. Found: C, 78.26; H, 7.70; P,9.42.

Preparation of 1-(1-Phenanthryl)-1,2,2,3,4,4-hexamethylphosphetanium Bromide (35). The 1.25g (0.0037 mole) of the oxide (34) in 50 ml of benzene was added 500 mg of triethylamine followed by 1g (0.oo74 mole) of trichlorosilane. The mixture was stirred for 5 hr. at room temperature and then brought to reflux for 4 hr.. The cooled mixture was treated with 50 ml of

20% sodium hydroxide solution. The organic layer was separated and washed with a saturated sodium chloride solution, dried over sodium sulfate and evaporated. The residue was dissolved in ether and treated with 5 ml of methyl bromide in a sealed flask. After 2 days, 1.34g (87% overall) of solid product was filtered. The salt was recrystallized from ethanol-ethyl acetate to produce a solid, m.p. 267-269°. The nmr ($DCCl_3$) showed peaks at: τ=0.75-2.92 (9H, m, aromatic), τ=7.21 (3H, d, $^2J_{PCH}$=12.5 cps), τ=8.15 (6H, d, $^3J_{PCCH}$=20.0 cps), τ=8.60 (6H, d, $^3J_{PCCH}$=18.5 cps), τ=8.75 (3H, d, $^3J_{HCCH}$=7.0 cps), τ=6.50 (1H, m). Anal. Calcd. for $C_{23}H_{28}BrP$: C, 66.50; H, 6.79; Br, 19.24. Found: C, 66.51; H, 6.69; Br, 19.16.

Alkaline Decomposition of (35). A solution of 1.09g (26 mmoles) of (35) in 20 ml of water was covered with 20 ml of benzene-chloroform (1:1) and stirred in an ice-bath. To the above solution was added dropwise 4 ml of 1 N sodium hydroxide solution over 15 min.. The mixture was stirred at room temperature for another 20 min. and the organic layer was separated, dried over anhydrous sodium sulfate and evaporated to a crude liquid. The nmr ($DCCl_3$) showed peaks at: τ=1.8-2.75 (6H, m, aromatic), τ=.60-4.70 (2H, m, vinyl), τ=6.08-6.47 (2H, m, allyl), τ=8.56 (3H, d, $^2J_{PCH}$=13.0 cps), τ=8.73 (3H, d, $^3J_{PCCH}$=15.0 cps), τ=8.92 (3H, s), τ=9.33 (3H, s), τ=9.08 (3H, d, $^3J_{HCCH}$=7.0 cps).

Preparation of (36). The crude product above was dissolved in 150 ml of decalin and treated with 500 mg of 30% Palladium over charcoal. The mixture was heated to reflux for 4 days during which a stream of nitrogen gas was bubbled through it. The resulting mixture was cooled, filtered and the catalyst was washed with benzene. The combined organic filtrates were concentrated in vacuo at 90° (10 mm) to reduce the total volume to 10 ml; cooling of the solution gave 310 mg of white precipitate which was filtered,

m.p. 211-216° (35% yield from the last two steps). The nmr ($DCCl_3$) showed peaks at: τ=0.50-2.77 (8H, m, aromatic), τ=8.28 (3H, d, $^2J_{PCH}$=11.5 cps), τ=8.93 (3H, d, $^3J_{HCCH}$=7.0 cps), τ=8.56 (3H, s), τ=8.72 (3H,s), τ=8.77 (3H, d, $^3J_{PCCH}$=14.0 cps), τ=8.72 (3H, d, $^3J_{PCCH}$=16.0 cps), τ=7.99 (1H, partially hidden). The above assignments were verified by P^{31} decoupling experiment.

The product was recrystallized from benzene-petroleum ether (30-60°) several times and sublimed at 175° (0.1 mm) to give the analytical sample m.p. 250-252°. Anal. Calcd. for $C_{23}H_{27}OP$: C, 78.83; H, 7.77; P, 8.84. Found: C, 79.00; H, 7.87; P, 8.80. Found: C, 78.83; H, 7.70.

Preparation of 1-(9-Phenanthryl)-2,2,3,4,4-pentamethylphosphetane-1-Oxide. A Grignard reagent was prepared from 53g (0.206 mole) of 9-bromophenanthrene and 5.5g (0.23g atom) of magnesium turnings in 500 ml ether-benzene.

The above Grignard reagent was added to a solution of 60g (0.3 mole) of the acid chloride (5) in ether solution over 2 hr. at 0° with stirring, under an atmosphere of nitrogen. The Gilman test was negative after 2 hr. The reaction was quenched with saturated ammonium chloride solution at 0° and the mixture was stirred overnight. The precipitate was filtered. The organic layer was treated with 100 ml of 10% sodium hydroxide solution with stirring for several hours, dried and evaporated. The residue was treated with ether-petroleum ether (30-60°) to give a solid. Both products were recrystallized from ethanol-water (Norit) to obtain 21.7g of the purified solid, m.p. 206-213°. (22%). The nmr ($DCCl_3$) showed peaks due to the major isomer at: τ=1.20-2.55 (9H, m, aromatic), τ=7.42 (1H, o, $^3J_{PCCH}$=3.0 cps, $^3J_{HCCH}$=7.0 cps), τ=8.41 (6H, d, $^3J_{PCCH}$=16.0 cps), τ=8.75 (6H, d, $^3J_{PCCH}$= 17.5 cps), τ=9.07 (3H, 2d, $^4J_{PCCCH}$=1.6 cps, $^3J_{HCCH}$=7.0 cps).

The compound was recrystallized several times from ethanol-water and then sublimed at 210° (0.05 mm) to give the analytical sample. Anal. Calcd. for $C_{22}H_{25}OP$: C, 78.54; H, 7.49. Found: C, 78.43; H, 7.47.

Reduction of the Oxide and Quaternization. A suspension of 16.8g (0.05 mole) of the above oxide in 500 ml of benzene was heated until the solid dissolved. To this solution at room temperature, was added 6g (0.66 mole) of triethylamine and 8g (0.06 mole) of trichlorosilane. The mixture was stirred at room temperature for 1 hr. and then refluxed for 4 hr.. The cooled reaction mixture was treated with 125 ml of 20% sodium hydroxide solution. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate and evaporated to give a solid residue, m.p. 105-108°. The residue was redissolved in ether and treated with an excess of methyl bromide. After allowing the reaction to stand for 24 hr., the salt was filtered to yield 18.0g of the product, m.p. 265-269°. Recrystallization from ethanol-ethyl acetate gave white crystals, m.p. 270-273°. The nmr ($DCCl_3$) showed peaks due to the major isomer at: τ=0.83-2.70 (9H, m, aromatic), τ=6.48 (1H, o, $^3J_{HCCH}$=7.0 cps, $^3J_{PCCH}$=2.0 cps), τ=7.18 (3H, d, $^2J_{PCH}$=13.2 cps), τ=8.08 (6H, d, $^3J_{PCCH}$=20.5 cps), τ=8.42 (6H, d, $^3J_{PCCH}$=18.5 cps), τ=8.89 (3H, d, broad). Anal. Calcd. for $C_{23}H_{28}BrP$, 19.24. Found: Br, 19.56.

Attempts to convert the above salt to the steroid precursor were unsuccessful. Although, the decomposition did occur, a glassy product was obtained. The product gave glassy masses after treatment of the crude product with Pd/ C in decalin.

Alkaline decomposition of 1-Phenyl-2,2,3-trimethylphosphetane 1-Oxide (37) to (38). To a mixture of 2.2g (0.01 mole) of the oxide (37) and o.8g (0.02 mole) of sodium hydroxide in 10 ml methyl cellosolve (filtered from

ferrous sulfate) was added 4-5 drops water, and the mixture was refluxed for 2 hr.. The solvent was evaporated, and the resulting brown semi-solid was treated with 15 ml water. The solution was extracted with two 20 ml portions of benzene. The aqueous layer was acidified with concentrated HCl which precipitated an oily liquid. The mixture was extracted with methylene chloride, and the combined extracts were dried over anhydrous sodium sulfate and evaporated to obtain 2.7g of a brown, oily liquid that solidified on scratching. Recrystallization from methanol-water gave 1.8g (75%) of acid, m.p. 92.5-96°. The nmr ($DCCl_3$) showed peaks at: τ=2.08-2.75 (5H, m, aromatic), τ=8.00-9.00 (1H, m), τ=9.02, (6H, d, $^3J_{PCCH}$= 17.0 cps) τ=9.12 (6H, d, $^3J_{HCCH}$=7.0 cps), τ=2.60 (1H, s). Anal. Calcd. for $C_{12}H_{19}O_2P$, 1/2 H_2O: C, 61.26; H, 8.57. Found: C, 61.68,; H, 8.23.

Alkaline decomposition of 1-Phenyl-2,2,3,3-tetramethylphosphetane 1-Oxide (39) to (40). To a mixture of 2.36g (0.01 mole) of the phosphine oxide (39) and 0.8g (0.02 mole) of sodium hydroxide in 10 ml methyl cellosolve was added 4-5 drops of water and the mixture was refluxed for 2 hr.. The solvent was evaporated and the residual brown liquid was dissolved in 15 ml water. The equeous solution was extracted with methylene chloride and then acidified with concentrated HCl. The precipitate was filtered to obtain 2.3g of a pale yellow powder. Recrystallization from methanol-water yielded 2.2g (86.5%) of the acid in two crops, each with m.p., 181-184°. The nmr ($DCCl_3$) showed peaks at: τ=2.06-2.75 (5H, m, aromatic), τ=8.98 (6H, d, $^3J_{PCCH}$=17 cps), τ=9.01 (9H, s), τ=1.70 (1H, s). Anal. Calcd. for $C_{13}H_{21}O_2P$: C, 64.98; H, 8.81. Found: C, 64.82; H, 8.66.

Reaction of 1-Chloro-2,2,3,4,4-pentamethylphosphetane 1-Oxide (5) with Phosphorus Pentasulfide. In a flask equipped with a water condenser fitted to a calcium chloride guard-tube, a mixture of 5.4g (0.027 mole) of the acid

chloride (5) and 2.2g (0.009 mole) of phosphorus pentasulfide was heated to 150° for 4 hr.. The mixture melted, darkened and a white solid deposited in the cold part of the condenser. The contents of the flask were sublimed in vacuo at 40° (0.2 mm) to produce 4.4g of crystalline solid with an adhering oil. Recrystallization from petroleum ether (30-60°) gave a crystalline solid (47) with a faint characteristic odor, m.p. 107-113.5°, yield 4.0g (69%). Repeated recrystallization raised the m.p. to 124-125.5°. The nmr (benzene) showed the compound to be a mixture of two isomers (2:1). The predominant isomer showed peaks at: τ=8.88 (6H, d, $^{3}J_{PCCH}$=22.0 cps), τ=8.86 (6H, d, $^{3}J_{PCCH}$=25.0 cps), τ=9.44 (3H, 2d, $^{3}J_{HCCH}$=7.0 cps, $^{4}J_{PCCCH}$= 1.0 cps), τ=8.01 (1H, m); and the minor isomer showed peaks at: 8.92 (6H, d, $^{3}J_{PCCH}$=23.0 cps), τ=8.79 (6H, d, $^{3}J_{PCCH}$=25.0 cps), τ=9.37 (3H, 2d, $^{3}J_{HCCH}$=7.0 cps, $^{4}J_{PCCCH}$=1.0 cps), τ=8.01 (1H, m). Anal. Calcd. for $C_8H_{16}ClPS$: C, 45.60; H, 7.65. Found: C, 45.94; H, 7.25.

Conversion of 1-Chloro-2,2,3,4,4-pentamethylphosphetane 1-Sulfide (47) to 1-Chloro-2,2,3,4,4-pentamethylphosphetane (48). A mixture of 25g (0.12 mole) of the compound (47) and 47.2g (0.234 moel) of tri-(n-octyl) phosphine was heated at 190-210° with stirring under a nitrogen atmosphere for 12 hr. in a three-necked flask equipped with a reflux condenser, a drying tube and a thermometer. The flask was connected to a distillation head. A stream of nitrogen (10-20 bubbles/ min.) was passed into the hot reaction mixture and the distillate over 40-93° was collected in an ice cold receiver (some solid that deposited in the condenser was collected by melting). The distillate was redistilled in vacuo at 36-38° (0.1-0.05 mm) using a 12" Vigreaux column to obtain a transparent colorless liquid, 12.6g (60%). The nmr (neat) showed the liquid to be a mixture of two isomers (2:1). The major somer (trans) exhibited peaks at: τ=8.77 (6H, d, $^{3}J_{PCCH}$=2.10 cps),

τ=8.88 (6H, d, $^3J_{PCCH}$=8.0 cps), τ=9.33 (3H, 2d, $^4J_{PCCH}$=1 cps, $^3J_{HCCH}$=7.0 cps), τ=7.22 (1H, 2q, $^3J_{PCCH}$=1.25 cps , $^3J_{HCCH}$=7.0 cps). The minor isomer showed peaks at: τ=8.70 (6H, d, $^3J_{PCCH}$=20.0 cps), τ=8.85 (6H, d, $^3J_{PCCH}$=6.0 cps), τ=9.29 (3H, 2d, $^4J_{PCCCH}$=1 cps, $^3J_{HCCH}$=7.0 cps), τ=7.84 (1H, 2q, $^3J_{PCCH}$=2.5 cps, $^3J_{HCCH}$=7.0 cps). Anal. Calcd. for $C_8H_{16}ClP$: C, 53.80; H, 9.03. Found: C, 53.91; H, 9.07.

Preparation of 1,1,2,3-Tetramethyl-3-butenylthiophosphonyl Dichloride (49). To a solution of 8.5g (0.04 mole) of the phosphine sulfide (47) in 100 ml of anhydrous benzene and 10 ml of petroleum ether (30-60°) at 0-5° was added 5.4g (0.04 mole) of sulfuryl chloride in 50 ml of benzene over 2 hr. with stirring under a nitrogen atmosphere. The mixture was stirred at room temperature for 24 hr.. A yellow oil separated at the bottom. Evaporation of the solvent followed by distillation of the residue from a 12" Vigreaux column in vacuo gave a colorless liquid, b.p. 49-51° (0.03-0.04 mm), 8.7g (89%). The nmr (neat) showed peaks at: τ=5.0-5.20 (2H, vinyl), τ=6.60-7.30 (1H, m,allyl), τ=8.58 (3H, d, $^3J_{PCCH}$=28.2 cps), τ=8.55 (3H, d, $^3J_{PCCH}$=28.8 cps), τ=8.72 (3H, d, $^3J_{HCCH}$=7.2 cps), τ=8.22 (3H, broad s). Anal. Calcd. for $C_8H_{15}Cl_2PS$: C, 39.19; H, 6.17; P, 12.63; Cl, 28.92. Found: C, 39.23; H, 6.23; P. 12.49; Cl, 28.95.

Preparation of a 1:9 (cis: trans) Mixture of Isomers of 1-Phenylphosphetane (41) was accomplished by Reduction of 1:19 (cis: trans) of the Oxide (20) Stereospecifically with $HSiCl_3$/Pyridine by the Method Described by Chrovat (2).

Stereospecific Oxidation of Phosphetane (41) with t-Butyl Hydroperoxide. To a stirred solution of 2.0g (0.011 mole) of the above prepared phosphetane (41) in 5 ml of benzene at 0-5° under nitrogen was added a solution of 0.91g t-butyl hydroperoxide (90%) in 15 ml benzene over 45 min.. The mixture was

stirred overnight without cooling. Evaporation of the solvent gave a crude solid (2.2g - 100%) of the crude oxide. A small amount of the product was sublimed in vacuo at 80° (0.2 mm). The nmr (benzene) showed the product to be a mixture of isomers (cis:trans::11:89) of (20) indicating that the oxidation reaction resulted in predominant retention of the configuration at phosphorus.

Quaternization of Chlorophosphetane (41) with Methyl Bromide. To 1.0g (0.0056 mole) of the chlorophosphetane in 5 ml of benzene was added 2 ml of methyl bromide and the contents were allowed to stand in a sealed flask for 4-days. A white precipitate formed. The ppt was filtered, and washed with benzene to obtain 1.3g of a crystalline solid (47.5%). Recrystallization from acetonitrile gave a solid, m.p. 225-242° (decomposition). The nmr ($DCCl_3$) showed peaks at: for the major isomer τ=8.57 (6H, d, $^3J_{PCCH}$= 18.0 cps), τ=8.66 (6H, d, $^3J_{PCCH}$=21.5 cps); minor isomer τ=8.49 (6H, d, $^3J_{PCCH}$=18.5 cps), τ=8.67 (6H, d, $^3J_{PCCH}$=22.0 cps), peaks common to both the isomers at: τ=7.82 (3H, d, $^2J_{HCH}$=12.5 cps), τ=8.97 (3H, 2d, $^3J_{PCCH}$=1.5 cps, $^3J_{HCCH}$=7.0 cps). Anal. Calcd. for $C_9H_{20}POBr$: C, 42.36; H, 7.90; P, 12.14; Br, 31.32. Found: C, 42.53; H, 7.89; P, 12.12; Br, 31.20; Cl, 0.00.

Treatment of the Hydroxyphosphetanium Salt with Ethyl Diazoacetate. To about 300mg of the salt covered with 10 ml of anhydrous ether was added 1 ml of ethyl diazoacetate. A slow evolution of gas occurred which became rapid on crushing the solid. After the effervescence ceased, the solution was injected into the glpc and the volatile products were identified as ether,ethyl diazoacetate and ethyl bromoacetate by comparison of retention times x to an authentic sample. The analysis was performed on the Varian A-90 instrument on a 20% SE 30 column. The remaining solution was evaporated under vacuum and the residual solid was identified as 1,2,2,3,4,4-hexamethylphosphetane

1-oxide (22) on the basis of the nmr of the product and that of an authentic sample.

CHAPTER II

STEREOCHEMISTRY OF NUCLEOPHILIC ATTACK ON CYCLIC PHOSPHORUS COMPOUNDS

1. Introduction

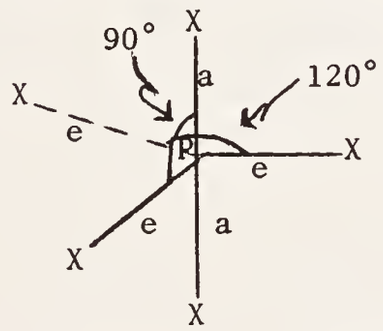
Organophosphorus compounds are subject to nucleophilic displacement reactions at the phosphorus site. Depending upon the geometry of the transition state, the reaction may lead to retention, recemization or inversion of configuration at the phosphorus. Available evidence points to inversion of configuration in most cases[44] and so the transition state for bimolecular reaction may be written as follows:

where X is the leaving group and N the nucleophile. In addition, there are reactions which are assumed to proceed through stable intermediates. In these cases, a pentacovalent intermediate may be formed which may either have trigonal-bypyramidal (60) or a tetragonal pyramidal geometry (61), depending upon whether the phosphorus in the intermediate is $sp^3d_{z^2}$ or $sp^3d_{x^2-y^2}$ hybridized (21). The geometry and the behavior of such intermediates may be explained on the basis of pentacovalent phosphorus compounds.

(60)

(61)

Calculation of the relative energies of structure (60) and (61) have shown (60) to be more stable than (61), [45,46] and indeed all PX_5 compounds known to date (where X is any monovalent substituent) have a trigonal-bipyramidal geometry. Evidence for this was not obtained until recently, since early electron diffraction data was inconclusive [47], and inference of the geometry was based mainly on spectroscopic evidence. It must also be pointed out here that in a PX_5 molecule of trigonal-bipyramidal geometry, the axial bonds should theoretically be longer than the equatorial bonds [48].



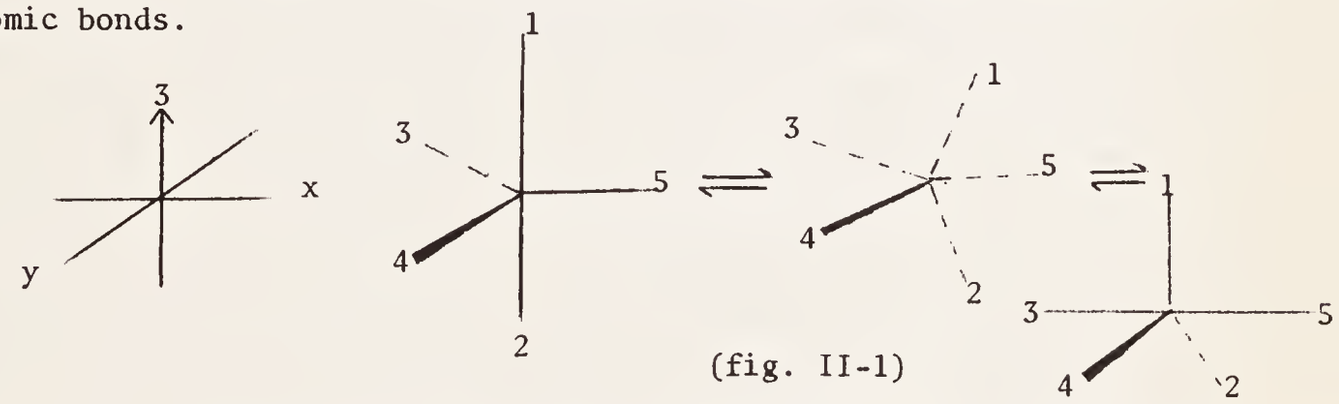
(62)

a= axial or apical bond
e= equatorial bond
x= F

Braune and co-workers [47] were the first to obtain the electron diffraction data on pentafluorophosphorane (2). They found that all the phosphorus-fluorine bonds in this compound were of equal length. This is not only contrary to the theoretical expectation but to spectroscopic and chemical evidence as well (see p. 52). Reinvestigation of the same compound (62) by Hansen and Bartell [49] (1.534 A°) were indeed found to be shorter than the axial bonds (1.577 A°). Prior to the latter results, all the structural assignments were based on spectral data. Thus, Gutowsky [50,51] on the basis of ir data had concluded that PF_5 had a trigonal-bipyramidal geometry. Holmes and co-workers [52,53] studied the temperature

^{19}F nmr and chlorine quadrupole resonance spectra of various compounds of the general formula PCl_nF_{5-n} where n=1,2,..5 and observed that all the compounds studied had trigonal-bipyramidal geometry. Recently, evidence for the geometry of various phosphorane compounds has been obtained through X-ray investigations [54].

Berry [55] first proposed a possibility of equilibration of substituents in a trigonal-bipyramidal PX_5 molecule and coined the term "pseudorotation" for the pnenomenon. This is defined as an intramolecular process in which a trigonal-bipyramidal molecule is transformed by deforming bond angles in a way, so that it appears to have been rotated by 90° about one of the interatomic bonds.



(fig. II-1)

In fig. 1, substituent 4, which is towards the viewer (along the Y-axis) remains fixed; whereas the apical substituents 1 and 2 are pushed backward and the equatorial substituents 3 and 5 are pulled forward so as to produce a tetragonal pyramid in which group 4 is at the apex. Continuing this process, a second trigonal bipyramid is produced which appears to have been produced by rotating the first trigonal bipyramid about the bond along the Y-axis in which groups 3 and 5 are apical and 1,2 and 4 are equatorial. The substituent about which a pseudorotation occurs is referred to as a 'picot' group (substituent 4 in the fig. 1). The tetragonal pyramid occurs as a transition state in this process because it is relatively higher in energy [46].

The positional exchange of substituents in trigonal-bipyramidal molecules by an intramolecular process was demonstrated in the classical research of Gutowsky, Schmutzler and Muetterties. Gutowsky [51] showed that the ^{19}F nmr of PF_5 exhibited only one doublet (^{19}F signal split by phosphorus, spin=1/2). This observation o the equivalence of fluorine atoms in PF_5 can be best explained by assuming one of the following:

i) a fortuitous overlap of two ^{19}F signals,

ii) valence-orbit hybridization,

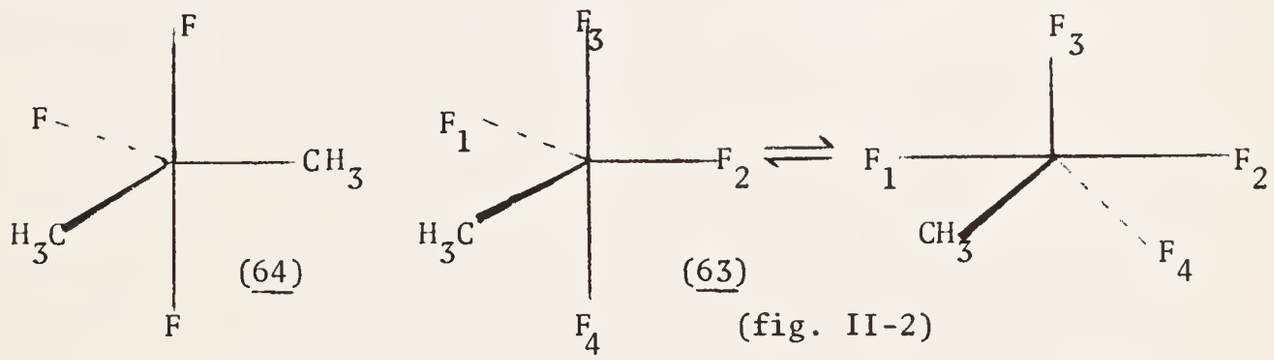
iii) a rapid positional exchange of substituents in a trigonal bipyramid.

The suggestion of accidental degeneracy was ruled out by Berry [55] on the following grounds: Downs and Johnson [56] have shown that phosphorus pentachloride exhibits a difference in the exchange rates with isotopically labelled chlorine at the equatorial vs. the axial sites. Berry argued that this shows a definite difference in the reactivity and hence, as a corollary; in the electron density at the two reaction sites. This example of difference in the electron density at the two sites in PCl_5 can be easily extrapolated to PF_5 and so overlap of the signals could have not occured.

The hypothesis of valence-orbit hybridization was first advanced by VanWazer and co-workers [57]. The calculations carried out the explain spectral data had some underlying assumptions which, as the authors pointed out were critical to the hypothesis advanced. It did not gain widespread support.

This leaves Berry's hypothesis of pseudorotation to be tested for its generality. Considerably more came to be known about pseudorotation as a result of the investigations by Schmutzler and Muetterties. For example, the nmr of methyltetrafluorophosphorane (63) shows only one kind of proton

and one kind of fluorine atom, a phenomenon which can be easily explained by invoking pseudorotation. However, dimethyltrifluorophosphorane (64) shows two kinds of fluorine atoms in the ratio 2:1 but only one type of methyl proton [58]. This can be explained by assuming that the two methyl groups occupy equatorial positions wheras one of the three fluorines occupies and equatorial site and the remaining two occupy apical positions. (fig. 2). The substituents do not equilibrate; which implies an absence of pseudorotation. A tetragonal pyramid could rationalize the nmr observations. However, Hansen and Bartell [59], in their electron diffraction investigations on (63) and (64), have not only shown that the molecules are trigonal bipyramids but also, that the methyl groups in both the systems occupy equatorial positions. The equivalence of the fluorine atoms in (63) can be easily rationalized by assuming that the methyl groups serves as a pivot in each pseudorotation allowing it to remain in the equatorial position. This has been shown in fig. 2, in which the fluorine atoms are numbered for convenience.



(fig. II-2)

Similar evidence for pseudorotation in the cyclic system tetramethylenetrifluorophosphorane (65) was obtained by Schmutzler during the temperature dependent ^{19}F nmr [58] investigation on the compound. However, he was unable to obtain any evidence for the equilibration of fluorine atoms in pentamethylenetrifluorophosphorane (66) (see p.55). The phenomenon of pseudorotation has also been observed in compounds which contain other hetero-

atoms, e.g., phenylarsenic tetrafluoride ($PhAsF_4$) [69].

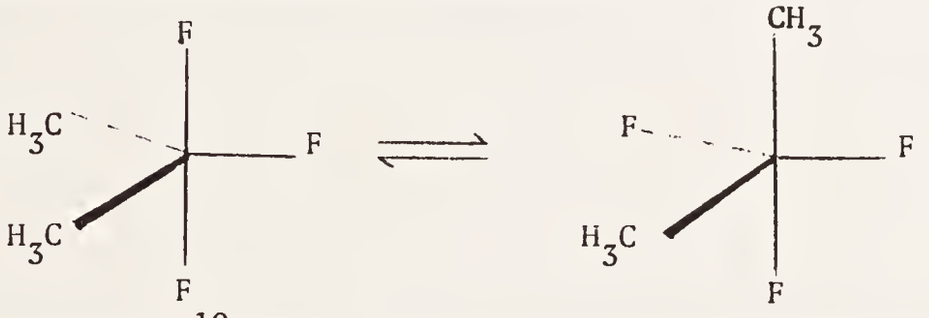
From the above discussion, it is not clear why (64) does not show any evidence of pseudorotation. In this case, for a pseudorotation to occur, one of the methyl groups must occupy an apical position. In order to explain the non-equivalence of fluorine atoms in (64), Muetterties [58] suggested that more electronegative groups preferentially occupy apical positions whereas less electronegative groups prefer equatorial positions. This allows for the placement of the methyl groups in equatorial positions in both compounds (63) and (64).

To invoke electronegativity as the basis of positional occupancy can be easily questioned, since steric factors alone may explain the observations. Triechel and co-workers [61] have advanced an interesting case against this argument. They showed that HPF_4 and DPF_4 show rapid positional equilibration of the substituent fluorines between -90 and -50°. On the other hand, the ^{19}F nmr of H_2PF_3 and D_2PF_3 show two different kinds of fluorine atoms in the ratio 2:1 at -46°. The downfield signal (intensity=2) arises from the two apical fluorine atoms in the equatorial position. By warming up to -15°, the peaks are observed to broaden and finally coalesce to a doublet supporting the view that the fluorine atoms experience a similar averaged environment by an intramolecular process. The P-F coupling remained constant indicating an absence of any significant contribution from an intermolecular process. The equatorial preference of hydrogen and deuterium conclusively rules out the positional preference due to steric factors alone.

The selectivity in positional occupancy and its relation to the electronegativity of the substituent can be rationalized on theoretical grounds [62,66]. Phosphorus in a trigonal bipyramid is sp^3d hybridized. Of these

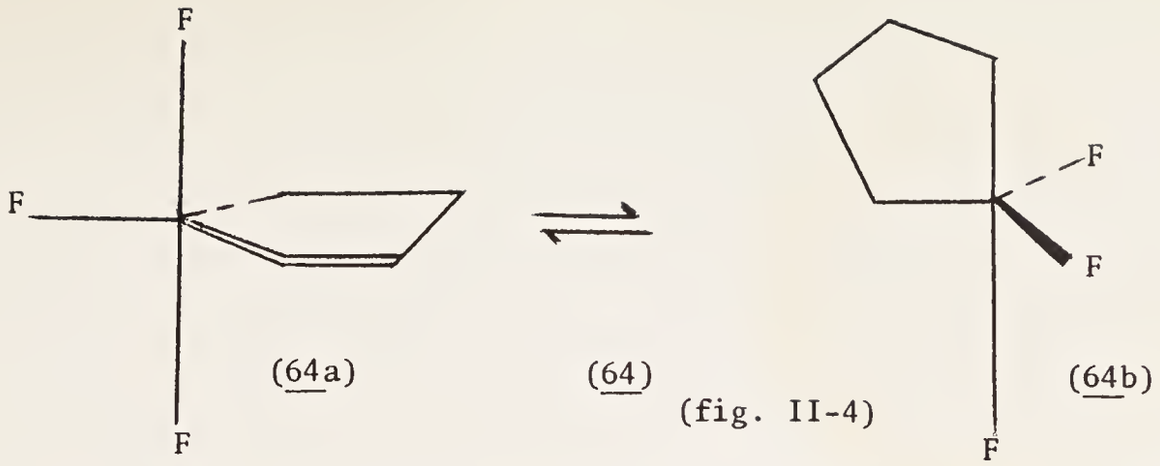
five spatially oriented hybrid bonds, the s- character is concentrated in equatorial bonds (sp^2 hybridization), rendering the equatorial bonds more electronegative. The axial-bonds do not have any s- character (pd hybridization) and so are more electropositive. As a result, more electronegative substituents prefer axial positions whereas less electronegative (more electropositive) substituents prefer equatorial sites.

On the above basis, it is easy to understand the nonequivalence of fluorine atoms in (64). As shown in fig. 3, for the equilibration to occur, one of the methyl groups must occupy an apical position to produce an energetically unfavorable intermediate:



(fig. II-3)

On the other hand ^{19}F nmr of compound (65) shows that all three fluorine atoms in the molecule are equivalent. Since H-F and P-F couplings remain constant, any contribution due to an intermolecular process can be ruled out. An intramolecular process such as pseudorotation may therefore be responsible. However, this cannot occur unless one of the P-C ring bonds is placed in an apical position-an energetically unfavorable situation. Schmutzler [67] has investigated this case in detail by studying the temperature dependent nmr of the compound. The $\Delta E^{\ddagger}$ for the process was estimated to be 7 kcal/mole. He proposed that one of the P-C bonds in the system can occupy an apical position since the energy of such a state is lowered due to the strain present in a five-membered ring. Thus, he proposed contributions from structure shown in fig. 4.



(64a) (64) (64b)

(fig. II-4)

Recent X-ray data shows that the internal C-P-C angle in a five-membered ring is about 95° [68,69], thus, contribution due to structures such as (64)in which the ring spans two equatorial positions can be neglected because the C-P-C angle will be forced to expand to 120°. A more convenient path for the pseudorotation to occur involves intermediates such as (65) in which the ring spans an equatorial-apical relationship. This can be seen easily in fig. 5, where the substituents have been labeled:

On the basis of this information, Muetterties formulated the following rules [60] which have become known as Muetterties' Rules [70]:

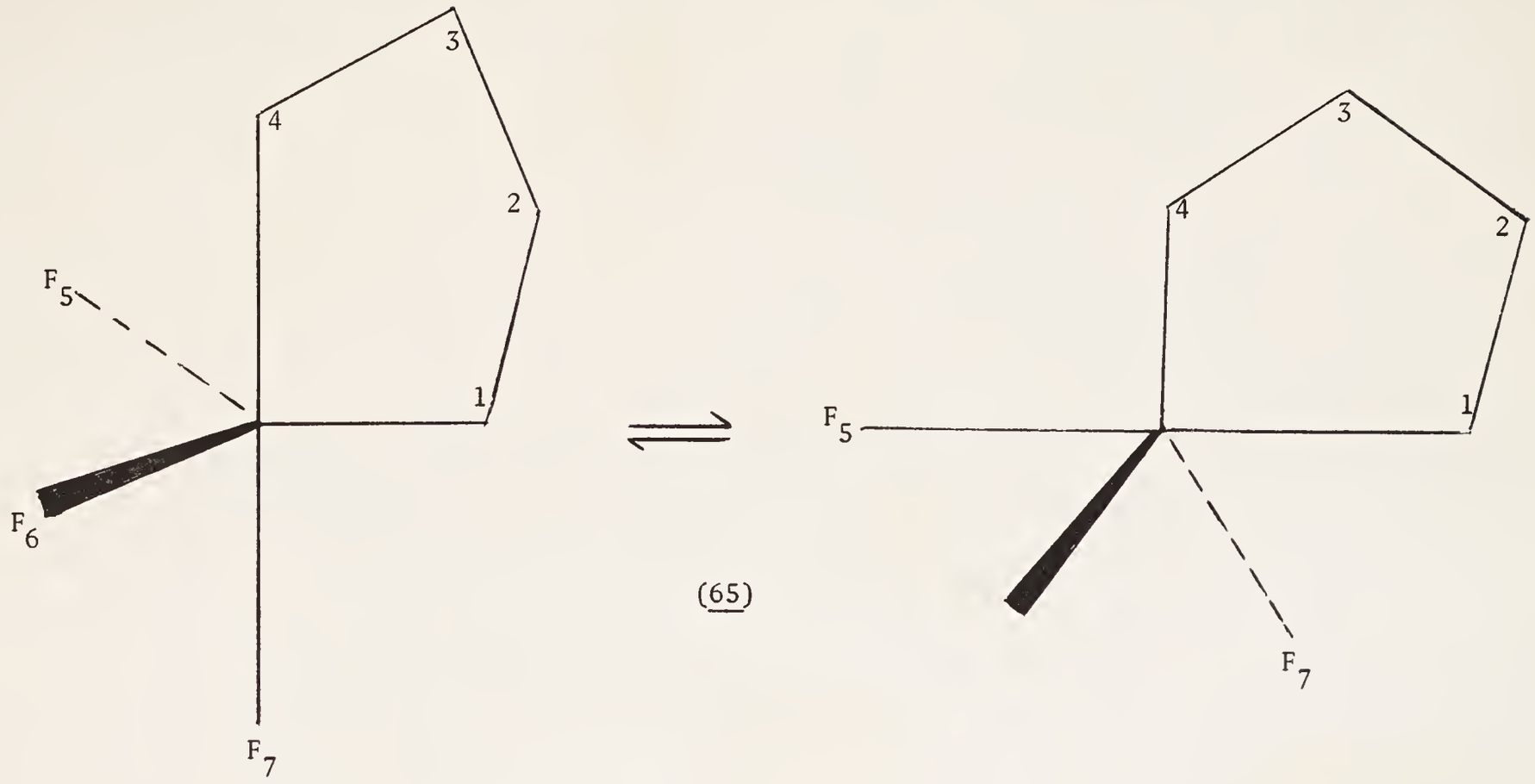
i. An intramolecular exchange of substituents in a trigonal bipyramid molecule can occur through pseudorotation,

ii. Electronegative substituents prefer apical positions,

iii. The preference in (ii), can be limited due to internal strain in the molecule,

In the light of the above generalizations, the application of the pseudorotation hypothesis can be readily understood.

After following through a few steps of pseudorotation in a particular system, it becomes obvious that the determination of the possibility for one of the steps to occur could be quite complicated. This could be less difficult when there are geometrical constraints (such as a small ring in the molecule) involved. An attempt has been made to simplify this process



(65)

Fig. II-5

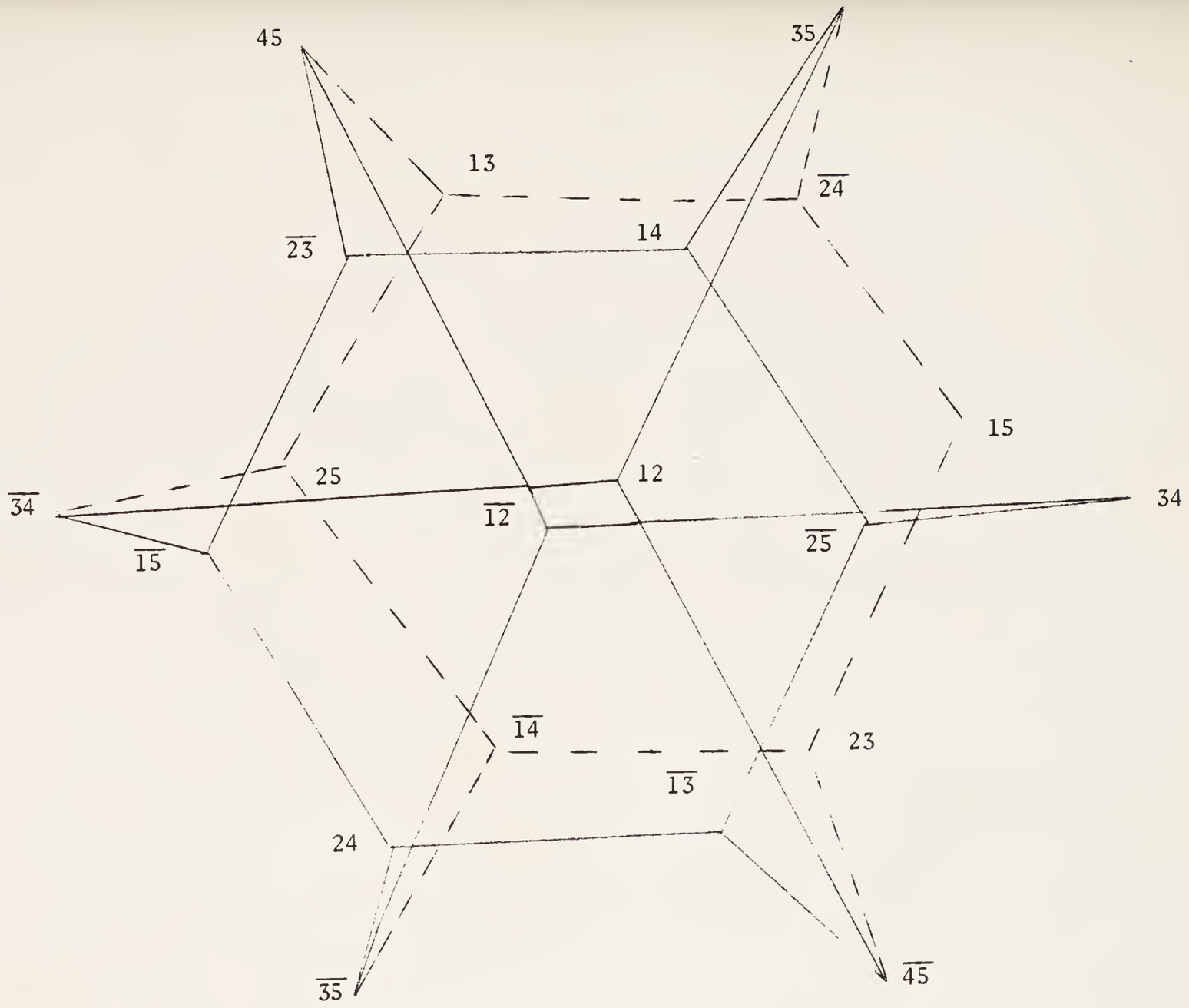
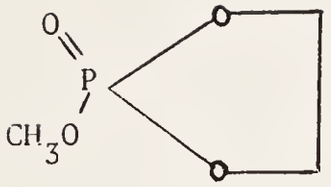


Fig. II-6. Projection of Balaban's 20-vertex Graph as Given by Mislow [73]. The index Numerials 1 and 2 are assigned to the termini of the phosphorus containing ring numbers 3,4 and 5 are arbitrary. $\overline{23}$ is the enatiomer of 23.

by various workers [71,73]. Cram [71] has given a diagram that can be utilized for the open-chain system. Mislow and co-workers [73] have described a very elaborate topological representation of the stereochemistry of the displacement reactions in phosphonium salts and similar systems. The requirement is that the reaction passes through a phosphorane intermediate. He has shown that the stereochemical outcome of such displacement reactions can be conveniently followed with the aid of a modified version of Balaban's 20-vertex graph which resembles the carbon skeleton of hexasterane (fig. 6). The eighteen vertices of the figure represent the eighteen stereoisomers of intermediate phosphorane trigonal bipyramid containing five different ligands. Two of these ligands are the termini of a ring system which are incapable of occupying the two apical positions. The pathways for the interconversion of isomers by pseudorotation are represented by twenty-four edges in fig. 6. A very interesting feature of the diagram is that in a D_{3h} represen tion, three planes intersect at the six-fold axis; each of the planes divides the graph into two subsets of nine vertices. Each subset represents the nine phosphoranes resulting from an external nucleophilic attack on a phosphorus atom of the given enatiomer of a cyclic phosphonium salt. As a result, the positions of the intermidiate phosphorane within sectors defined by two intersecting planes gives the stereochemical outcome of the reaction. The figure is a general one and too complex to be described here. Wislow has described a number of applications of this topological representation [73].

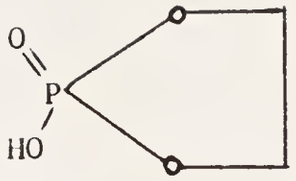
Although the convenient device discussed above will not be specifically used in the discussion which follows, it is valuable for following the course of a reaction in these rather complicated systems. At this point therefore, a few systems which undergo nucleophilic substitution to



(67)

$(CH_3O)_3 P = O$

(68)



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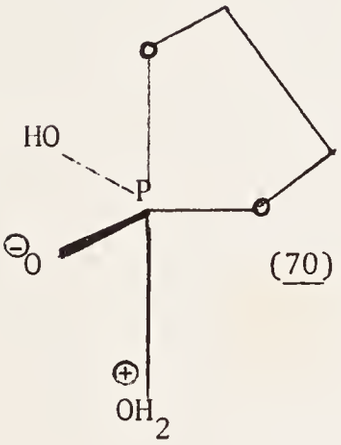
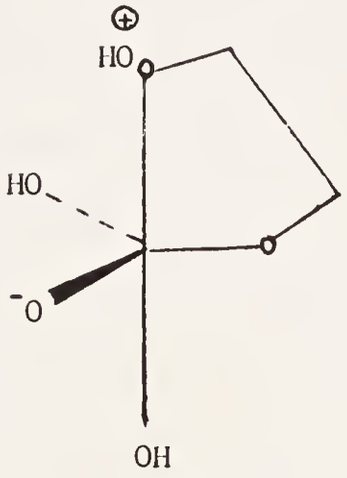
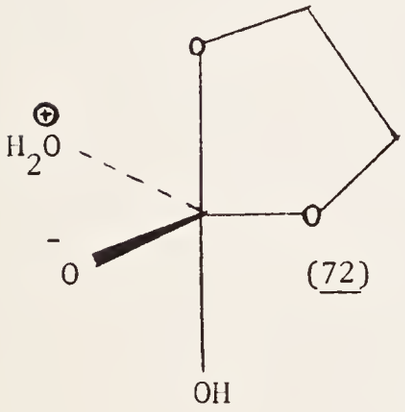


(70)



(71)



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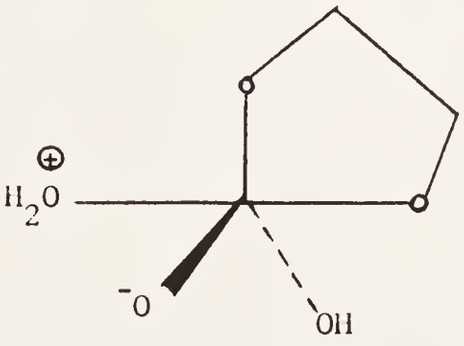


(73)

Fig. II-7.

yield a phosphorane intermediate capable of undergoing pseudorotation will be discussed.

Westheimer [74] found that the hydrolysis of methyl ethylene phosphate (67) with ring opening proceeds nearly 10^8 times faster than trimethyl phosphate (68). More important is the fact however, that the acid catalyzed exocyclic cleavage of themethoxy group occurs 10^6 times faster than (68). Haake and Westheimer [75] also observed that acid catalyzed hydrolysis of hydrogen ethylene phosphate (69) results in a rapid ^{18}O exchange in the unreacted ester. The enormously fast rate of ring opening can probably be rationalized in terms of the ring-strain in the cyclic ester. Difficulty is encountered in explaining the almost equally fast rate of exocyclic hydrolysis without ring opening. Apparently, the strain in the ring cannot possibly explain the rapid hydrolysis external to the ring. This problem of accounting for this unusual behavior will be dealt with in some detail because it will invoke some basic assumptions which will be necessary for this work.

Westheimer [75] advanced an argument that there ought to be a single mechanism which could account for all the observations. He made the following assumptions:

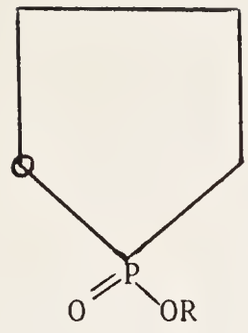
i. the reaction proceeds through a trigonal-bipyramidal intermediate with the ring spanning one apical and one equatorial position,

ii. the entering and leaving groups do so from an apical position (extended principle of microscopic reversibility). Justification for this argument is dealt with in detail (p.69).

With the aid of these assumptions and the possibility of pseudorotation of the intermediate phosphorane, Westheimer extended the following explanation [35]. Addition of a molecule of water on (69) should result in the formation of the intermediate (70). This process is favored because of the ring strain in the ester (see fig. 7). Protonation of this intermediate will give (71) which can then ring open by an apical departure. The protonation at the hydroxy oxygen will give another intermediate (72) which cannot give the observed 18_0 exchange if rule (ii) above were followed. Pseudorotation of (72) to yield (73) followed by departure of the molecule of water from the apical position will explain the 18_0 exchange.

The above discussion will help rationalize both the fast ring opening as well as fast rate of $^{18}0$ exchange and the dydrolysis external to the ring. The rationale is as follows: the ring spans one apical and one equatorial position in the intermediate which involves a C-P-C ring angle of 90°. Formation of the intermediate results in the reduction of the strain in the starting material. Since this intermediate can both hydrolyze with ring opening as well as with $^{18}0$ exchange; the fast reactions can be explained on the basis of the strain in the molecule because formation of the intermediate is facilitated due to the strain. It is assumed that the water and methanol molecules are not very different since exchange involves entering and leaving of the former whereas the exocyclic hydrolysis requires entering of the former and departure of the latter.

Recently, Boyd [76] has carried out molecular orbital calculations on cyclic and acyclic phosphate esters. He verified the above explanation for the fast rate of hydrolysis of the cyclic ester. The energy barrier for pseudorotation of the intermediate phosphorane was estimated to be about 12-15 kcal/mole as an upper limit.



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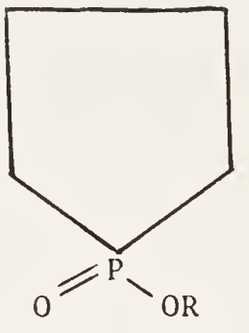

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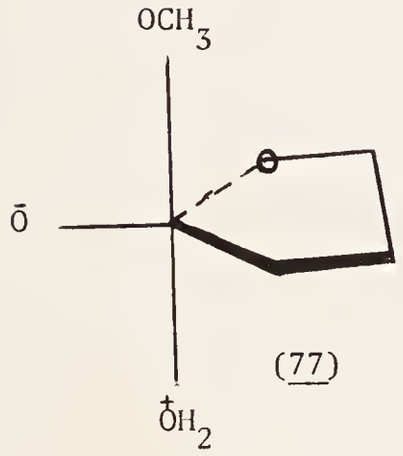

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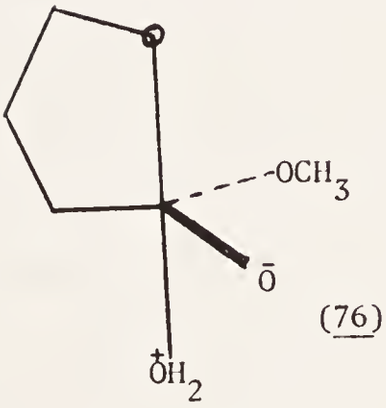

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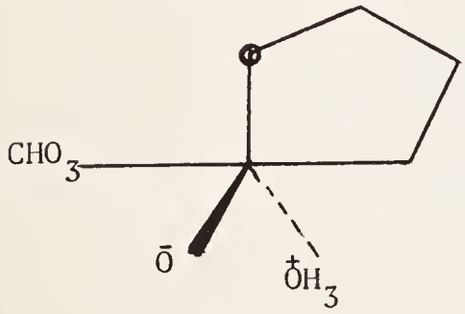

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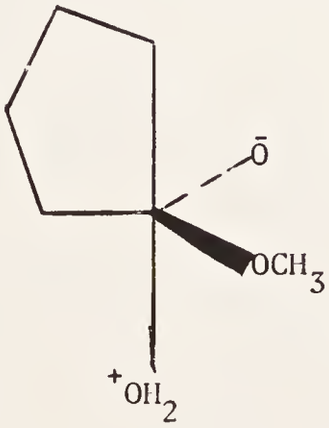

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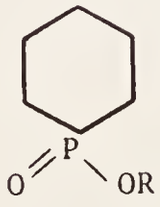
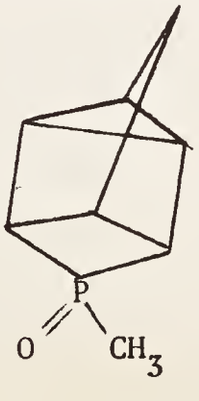


(80)

Fig. II-8.

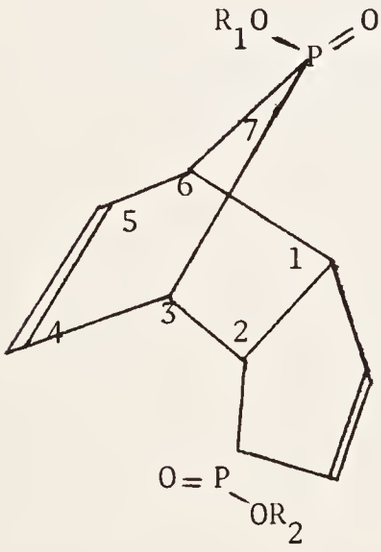
This hypothesis can be further applied to the hydrolysis of the phostonate (74) and the phosphinate (75) esters, both of which involve a five-membered ring (fig. 8). In case of (74), it was observed that the hydrolysis resulted in almost exclusive ring cleavage [77]. This can be explained on the basis of the positional preference rules of Muetterties. An attack by a molecule of water on (74) will preferably give the intermediate (76) which can hydrolyze with ring opening [77]. Intermediate (76) can also pseudorotate to give either (77) or (78). The formation of (77) can be ruled out because it will result in the expansion of the C-P-C ring angle to 120° and thus will be energetically unfavorable. Intermediate (78) on the other hand is not favored because it has an electronegative oxygen atom in an equatorial position whereas an electropositive methylene group in the apical position as in the intermediate (79). The energy for such a process may be so high that the reaction may not even go through a phosphorane intermediate. This has been confirmed by Aksnes and coworkers [78] who showed that (75)hydrolyzes with about the same rate as the six-membered ring phosphinate ester (80) as well as the open-chain analogue.

The restriction of the positional preference due to the strain in the molecule as mentioned in Muetterties' rules can be further supported by the fact that the highly strained phosphine oxide (1) undergoes a rapid ^{18}O exchange [79]. Most phosphine oxides fail to undergo exchange or do so extremely slowly. Once again, a phosphorane intermediate undergoing pseudorotation may be proposed as shown below:

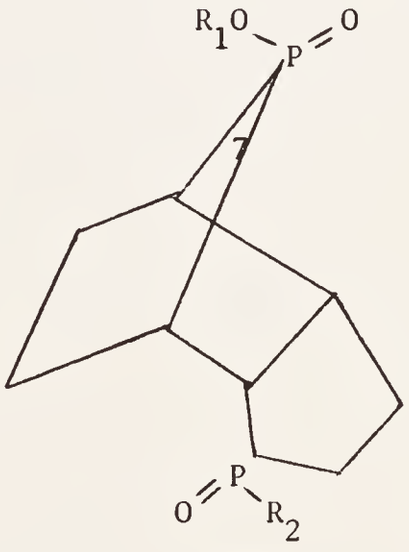


(1)

Westheimer [70,80,81] has demonstrated a very interesting example of pseudorotation during the hydrolysis of the bicyclic esters (81,82). One of the ester groups in these compounds hydrolyzed very rapidly compared to other open-chain or cyclic phosphinate esters. He argued that by analogy with bicycloheptane derivatives the bond angle at the 7- position of the bicyclic systems must be constricted. As a result of this angular strain, the hydrolysis could occur through the formation of a phosphorane intermediate followed by pseudorotation of the intermediate. Recent X-ray data reported by Lipscomb [69] corroborated the assumption of the strain in the molecules; the internal C-P-C angle was shown to be 87°. Thus, in these cases also, the relief of the strain achieved in going from the starting material to the intermediate is sufficient to overcome the positional preference.



(81)



(82)

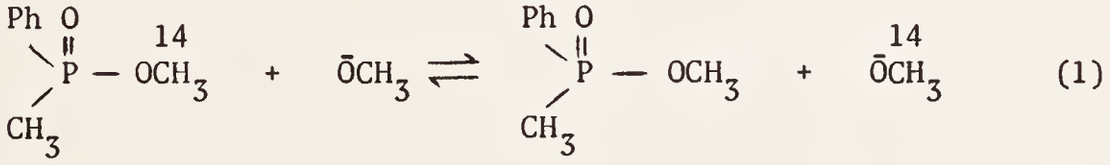
2. Hydrolysis of Phosphinate Esters

Results and Discussion. It is apparent from the previous discussion, that internal strain in five-membered ring systems has, in some cases, led to the verification of the pseudorotation hypothesis.

The four-membered ring compounds, due to larger strain (C-P-C = 83°) (page 17, present a very interesting system for testing the theory of pseudorotation and its consequences.

The most important assumption is that the molecule is sufficiently strained so that the barrier for the placement of the P-C ring bond in the apical position of the intermediate may be overcome by the relief of strain achieved in going from the starting material to the intermediate. It is therefore critical to demonstrate [70] that the reactions under investigation proceed through intermediates that are capable of undergoing pseudorotation.

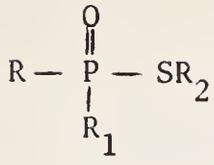
Nucleophilic reaction at a phosphoryl center is known to proceed through a transition state and results in overall inversion of configuration at phosphorus [44]. The mechanism, by analogy with the nucleophilic substitution at a carbon center, is called S_N2P (Substitution Nucleophilic Bimolecular at Phosphorus). A classical demonstration of inversion at a phosphoryl center was given by Green and Hudson [82]. They showed that the optically active ^{14}C labelled phosphinate ester (83) equibrated with its unlabelled analogue in methanolic sodium methoxide - (eq. 1):



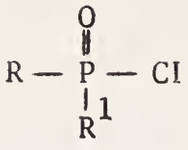
(1)

(83)

The rate of racemization was shown to be twice the rate of loss of ^{14}C label from the ester. Similarly, Green and Hudson [83] have shown that nucleophilic reactions on thiol esters (84) and phosphorochloridates (85) also occur with inversion of configuration.

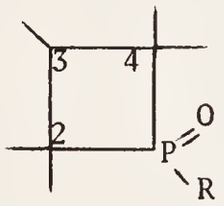


(84)



(85)

It was of interest to determine whether the stereochemistry of the above open-chain systems applied to the four-membered ring phosphinate esters. For this purpose, the reaction of sodium methoxide with the cis and trans isomers of ester (86) was examined.



(86)

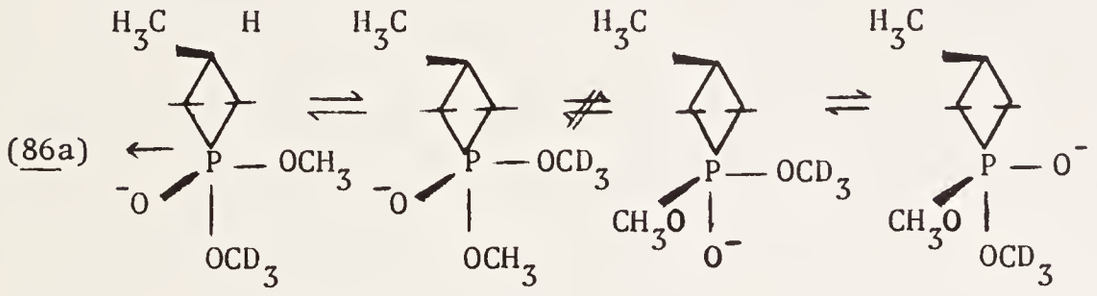
a : 3 CH_3 and R, (trans)

b : 3 CH_3 and R, (cis)

A methanolic solution of ester (86 a) and a mixture of 86 a and b (2:3) (R = OCH_3 in each case) were separately treated with sodium methoxide solution in evacuated, sealed nmr tubes. Heating to 50° did not show any significant change in the ratio of isomers as determined by nmr integration. Methanolic solutions of (86 a) and (86 a and b) (2:3) (R=OCD_3) were similarly treated with sodium methoxide. Exchange of OCD_3 by OCH_3 took place in each isomer. Since exchange of isomers occurred with out any isomer crossover, it was concluded that nucleophilic substitution with methoxide ion on the phosphinate ester (86) proceeded with retention of configuration [33].

The observation above, can be rationalized in terms of pseudorotation of the pentacovalent intermediate. Attach of methoxide ion on (86 a R=OCD_3) along the P-C bond from the apical position leads to intermediate (87) All

arguments used for (86 a) are equally applicable to (86 b). Pseudorotation of (87) with oxygen as a pivot will lead to (88), while employment of the deuteriomethoxy group as a pivot will yield (89). Both (88) and (89) are rotated in order to aid in visualization. Intermediate (88)can



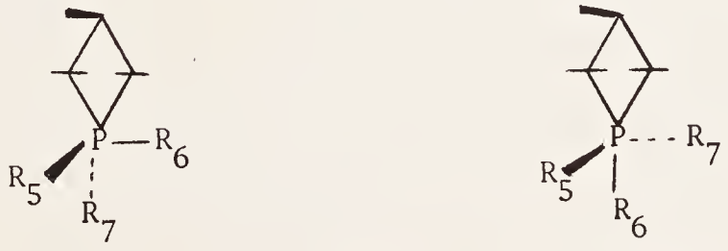
(88) (87) (89) (90)

decompose with the $-OCD_3$ group departing from the apical position (microscopic reversibility) to yield the same isomeric trans ester. Intermediate (89) will be higher in energy than (87) and (88)(which should be similar in energy) since (89) has a negatively charged oxygen atom in an apical position. According to Muetterties rules [55], O^- is less electronegative than the neutral O atom and should preferably occupy an equatorial position. Furthermore, (89) can undergo pseudorotation to yield either (87) or (90) which subsequently could decompose to yield isomer crossover which was not observed.

The same argument can be applied to the case of equatorial attack and equatorial departure. The methoxide ion can attack along the $P-C_2$ bond to yield the mirror images (*) of (88) and (90) depending upon whether the attack occurs from the same or the opposite side of the 3-methyl group.

(*) The attack along the $P-C_4$ bond will produce the object of the mirror image and therefore no optical acitivity is generated during the process.

Pseudorotation of the mirror image of (88) with 0^- as pivot yields the mirror image of (87) which on departure of the $-OCD_3$ group from an equatorial position should render the starting trans ester. The major reason for ruling out equatorial attack and departure is based on the consideration of the principle of least motion [84]. Stated in terms of Rice and Teller [81], "those elementary reactions will be favored that involve least change in atomic positions and electronic configuration." The transition state for apical and equatorial departure (or attack) are shown in fig. 9. In the following argument the angles in the phosphorane intermediate are assumed to be the same in an idealized trigonalbipyramid; whereas those in the ester are assumed very similar to the phosphine oxide (R=Ph)[30]. For apical departure, bonds $P-R_5$ and $P-R_6$ will have to change by about 20° (fig. 9) [33]. On the other hand, during the equatorial departure bonds $P-R_5$ will be altered 20° whereas bond $P-R_6$ will have to be transformed 60-70°. Although both paths should lead to the same results, only an apical in-out mechanism is favored because the molecule will go through the least deformation in this process.



(Fig. II-9)

Having demonstrated that nucleophilic substitution on the phosphinate ester (86) proceeded via an intermediate that can undergo pseudorotation, it seemed appropriate to investigate the rates of alkaline hydrolysis of these esters. In the event that the reaction goes through an intermediate, it would be expected that hydrolysis external to the ring will be fast.

Table 1 shows the rate data in the case of esters (8), (11), (15) and (86). A comparison shows that phosphinate ester (15) hydrolyzes 2300 times faster than (86). The unsymmetrical tetramethyl substituted ester (11) and and pentamethyl ester (8) hydrolyze at about the same rate but do so about as fast as (86). Structurally, (8) and (86) each have one additional methyl group in the 2-position relative to (15)and (11), respectively. However, the ratio of the rate constants are: (11)/(86) = 4, whereas (15)/(8) =1100. The reason for the difference seems to be steric in origin. To understand the nature of the proposed steric effect, examination of data in table 2 is necessary [86]. It can be seen that the estimated realtive rates in the phosphonate esters (91) when R=Et, i-Pr and t-Bu are 200: 7:1. On the other hand, the same change in the phosphinate esters (92) R= Et, i-Pr, t-Bu) produces the relative rates of hydrolysis are 10^5 :500:1. Trippett et al., [86] have argued that the dramatic rate differences between the substances with only one bulky group and those with two such groups are due to the steric hindrance in the transition state leading to the intermediate phosphorane. They further argued that, of two bulky t-Bu groups in the molecule, one must occupy an equatorial position. As a result, the steric hindrance in phosphinates with two bulky groups is more effective in blocking the approach of the in-coming nucleophile and consequently decelerates the rate of hydrolysis in these compounds.

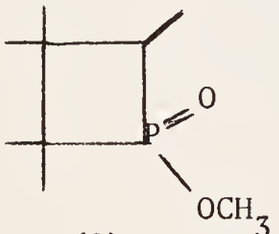
The argument outlined above seems to be valid in the cyclic systems in which the reaction must go through an intermediate as shown earlier. Its application to the open-chain systems is questionable since the available evidence indicates that nucleophilic substitution in such open-chain systems goes through a transition state rather than an intermediate [82].

In any event, Trippett's hypothesis of steric blocking of nucleophi-

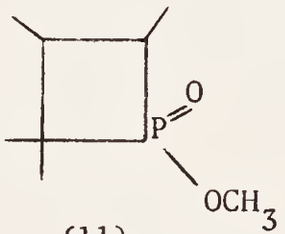
Table II-1. Alkaline Hydrolysis of Phosphinate Esters
Second-Order Rate Constants at 25°.

Compound	k_2 ($M^{-1}Sec.^{-1}$)
(8)	$2.51 \pm 0.06 \times 10^{-4}$
(11)	$1.96 \pm 0.065 \times 10^{-4}$
(15)	$1.51 \pm 0.012 \times 10^{-1}$
(86)	$5.85 \pm 0.13 \times 10^{-5}$

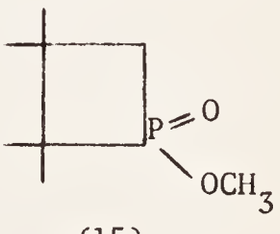
Compound	K_2 ($M^{-1}Sec.^{-1}$) at 45°
(15)	5.9×10^{-1} (Extrapolated)
(93)	3.9×10^{-1} (Ref. 82)



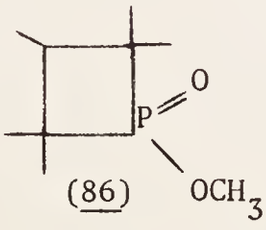
(8)



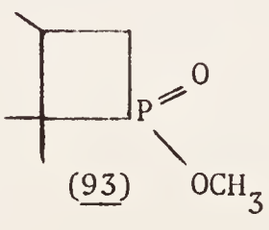
(11)



(15)



(86)



(93)

Table II-2. Alkaline Hydrolysis of Phosphonate and Phosphinate Esters - Second Order Rate Constants

$RP(:O)(OEt)_2$ (91)	
R	k_2 ($M^{-1}Sec.^{-1}$)
Et	7.4×10^{-3} (120°) *
i-Pr	4.4×10^{-4}
t-Bu	6.0×10^{-5}

$R_2P(:O)OEt$ (92)	70°	120°
Et	2.6×10^{-4}	
i-Pr	9.8×10^{-7}	4.1×10^{-5}
t=Bu		8.0×10^{-8}

* Calculated

Ref.: S. Tripett and W. Hawes , Chem. Comm., 577 (1968).

lic attack during the formation of the intermediate can be applied to the cyclic phosphinates. This can be clearly seen in the relative rates of (15) and (86). There are obviously two effects which are working in opposite directions: a) ring strain would lead to facile formation of the intermediate, which in turn would be reflected in acceleration of the rate of hydrolysis; b) steric blocking of the attacking reagent (noepentyl effect) [87] would result in deceleration of the reate of hydrolysis. In the case of (86)therefore, the rate of hydrolysis is faster than for (92)(R= t-Bu); however, the dramatic effect of rate acceleration is reflected in the compound (15) in which steric hindrance is not able to overcome the effect due to the ring strain.

Another interesting feature in table 1 is the relative rates of compounds (8) and (11); compound (8) which has an additional methyl group in position 3 hydrolyses slightly faster than (11). The reason for this small rate acceleration is not entirely clear. The same is true for (15) and (93).

One possible explanation is based on the conformational differences in the compounds. In (11) there is only one methyl group at position 3 which because of the puckering of the ring may stay as far from the reaction site as possible. In (8), on the other hand, there are two methyl groups in position 3 and as a result, one methyl group is always near the reaction site. (buttressing effect). This would raise the energy of the ground state and would thus account for the increased rate of hydrolysis. The $\Delta H^{\ddagger}$ values reflect this possibility since in (8), less energy would be required to reach the intermediate as shown below:

It should be mentioned that Bergesen[88], has claimed to have isolated two isomeric acids derived from the ester (86 R=Et). It is difficult to understand the claim of isolating isomeric acids in view of the possible tautomerization of the acid in solution:

The rates given in this work as well as those of Trippett[86] seem to be compatible with the trans isomer of the ester.

b. Experimental. The alkaline hydrolysis of the esters (8), (11) and (86) was followed by a titration procedure. Equal volumes of the required ester and alkali solutions were separately equilibrated in a double chambered flask in a constant temperature bath. The solutions were mixed. A 5 ml aliquot was withdrawn at intervals and quenched with a known volume of standard hydrochloric acid solution. The excess of the acid was titrated against a standard sodium hydroxide solution using phenolphthalein as an indicator.

In the case of the ester (15), the course of the reaction was followed by conductivity measurements. In a constant temperature bath, 0.04 molar solutions of the ester and alkali were separately equilibrated. Equal volumes of the solutions were mixed in a conductivity cell in a constant temperature bath. The resistance of the reaction mixture was determined at intervals with a conductivity bridge (model RC 1B, Industrial instruments). The calculations were performed as shown below (89):

$$t=(1/ak)\ [(R - R_o)/R_o]\ [\ R/(R_\infty - R)]\ - 1/ak$$

where t=time

a = initial concentration

Ro = Resistance at time = o

R = resistance at time = t

R_∞ = resistance at time

and

k = rate constant.

Table II-3. Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethyl-phosphetane 1-oxide (8)at 25.4°. A_o=0.03776 M. B_o = 0.02925 M.

#	time hr.	Conc. NaOH B	log AB_o/A_oB
1	0.278	2.906×10^{-2}	0.004
2	6.0	2.337×10^{-2}	0.2240
3	18.0	1.730×10^{-2}	0.0595
4	24.0	1.409×10^{-2}	0.0895
5	42.0	1.028×10^{-2}	0.1443
6	66.0	6.695×10^{-3}	0.2345

$k_2 = 2.66 \times 10^{-4} \pm 7.1 \times 10^{-6}$ M.$^{-1}$ Sec.$^{-1}$

$k_2 = 2.66 \pm 0.071 \times 10^{-4}$ M.$^{-1}$ Sec.$^{-1}$

Table 11-4. Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethyl-phosphetane 1-oxide (8) at 25.5°. A_o=0.0372 M., B_o= 0.0196 M.

#	Time hr.	Conc. NaOH	log AB_o/A_oB
1	9.0	1.428×10^{-2}	0.07o1
2	15.5	1.153×10^{-2}	0.1235
3	36.0	7.043×10^{-3}	0.2648
4	45.0	6.347×10^{-3}	0.2978
5	59.5	4.644×10^{-3}	0.4014
6	70.5	3.909×10^{-3}	0.4615
7	79.5	3.367×10^{-3}	0.5153

$k_2 = 2.273 \times 10^{-4} \pm 5.5 \times 10\text{-}6$ M.$^{-1}$ Sec.$^{-1}$
$= 2.27 \pm 0.055 \times 10^{-6}$ M.$^{-1}$ Sec.$^{-1}$

Table II-5. Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethyl-phosphetane 1-oxide (8) at 25.4°. A_o-0.0413 M., B_o = 0.0260 M.

#	Time hr.	Conc. NaOH	log B_oA/A_oB
1	9.0	1.834×10^{-2}	0.0626
2	18.0	1.358×10^{-2}	0.1265
3	24.5	1.138×10^{-2}	0.1688
4	45.0	6.850×10^{-3}	0.3086
5	54.0	5.960×10^{-3}	0.3512
6	69.0	4.528×10^{-3}	0.4402
7	80.0	3.754×10^{-3}	0.5042

$k_2 = 2.59 \times 10^{-4} \pm 5.25 \times 10^{-6}$ M.$^{-1}$ Sec.$^{-1}$.
$= 2.59 \pm 0.0533 \times 10^{-4}$ M.$^{-1}$ Sec.$^{-1}$.

Table II-6. Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethyl-phosphetane 1-oxide (8) at 60°. A_o = 1.11 x 10^{-1} M., B_o = 5.35 x 10^{-3} M. Pseudo-unimolecular reaction.

#	Time min.	Conc. NaOH B, M.	log B
1	8.0	4.401 x 10^{-3}	-2.3564
2	16.0	3.648 x 10^{-3}	-2.4379
3	24.0	3.110 x 10^{-3}	-2.5072
4	40.0	2.318 x 10^{-3}	-2.6349
5	56.0	1.868 x 10^{-3}	-2.7286
6	80.0	1.340 x 10^{-3}	-2.8729
7	104.0	1.183 x 10^{-3}	-2.9270

k_2 = 2.09 $\pm$ 0.17 x 10^{-3} M.$^{-1}$ Sec.$^{-1}$

Table II-7. Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethyl-phosphetane 1-oxide (8) at 60°. A_o = 1.11 x 10^{-1} M., B_o = 5.35 x 10^{-3} M. Pseudo-unimolecular reaction.

#	Time min.	Conc. NaOH B, M.	log B
1	8.0	4.421 x 10^{-3}	-2.3545
2	16.0	3.668 x 10^{-3}	-2.4355
3	24.0	3.159 x 10^{-3}	-2.5005
4	40.0	2.347 x 10^{-3}	-2.6295
5	56.1	1.819 x 10^{-3}	-2.7402
6	80.0	1.340 x 10^{-3}	-2.8729
7	104.0	1.066 x 10^{-3}	-2.9722

k_2 = 2.23 x 10^{-3} $\pm$ 1.36 x 10^{-4} M.$^{-1}$ Sec.$^{-1}$
= 2,23 $\pm$ 0.140 x 10^{-3} M.$^{-1}$ Sec.$^{-1}$

Table II-8. Activation Parameters for the Alkaline Hydrolysis of 1-methoxy-2,2,3,3,4-pentamethylphosphetane 1-oxide (8) in water.

Temperature °T	k_2(Average) M^{-1} Sec.$^{-1}$	$\Delta H^{\ddagger}$ kcal/mole	$\Delta S^{\ddagger}$ c.u.
298.5	2.51×10^{-4}		
		11.6	-36.1
333.1	2.16×10^{-3}		

Table II-9. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 25.1°. $A_o = 1.254 \times 10^{-1}$ M., $B_o = 5.001 \times 10^{-3}$ M. Pseudounimolecular reaction.

#	Time 10^3 Sec.	Conc. NaOH B, M.	log B
1	10.0	3.835×10^{-3}	-2.4162
2	15.0	3.355×10^{-3}	-2.4744
3	20.0	2.845×10^{-3}	-2.5459
4	26.0	2.480×10^{-3}	-2.6055
5	33.0	2.105×10^{-3}	-2.6768
6	41.0	1.771×10^{-3}	-2.7518

$k_2 = 1.98 \times 10^{-4} \pm 7.1 \times 10^{-6}$ M.$^{-1}$ Sec.$^{-1}$

$1.98 \pm 0.071 \times 10^{-4}$ M.$^{-1}$ Sec.$^{-1}$

Table II-10. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 25.1°. A_o = 1.254 x 10^{-1} M., B_o = 5.001 x 10^{-3} M. Pseudounimolecular reaction.

#	Time 10^3 Sec.	Conc. NaOH B, M.	log B
1	14.0	3.387 x 10^{-3}	-2.4702
2	22.0	2.730 x 10^{-3}	-2.5638
3	27.0	2.365 x 10^{-3}	-2.6262
4	30.0	2.209 x 10^{-3}	-2.7011
5	36.0	1.990 x 10^{-3}	-2.7011
6	40.0	1.792 x 10^{-3}	-2.7466
7	46.0	1.521 x 10^{-3}	-2.8179

k_2 = 1.94 x 10^{-4} ± 6.00 x 10^{-6} M.$^{-1}$ Sec.$^{-1}$
= 1.94 ± 0.06 x 10^{-4} M.$^{-1}$ Sec.$^{-1}$

Table II-11. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 39.65°. A_o = 1.218 x 10^{-1} M., B_o = 5.035 x 10^{-3} M. Pseudounimolecular reaction.

#	Time 10^2 Sec.	Conc. NaOH B, M.	log B
1	18.0	4.474 x 10^{-3}	-2.3493
2	36.0	3.805 x 10^{-3}	-2.4196
3	54.0	3.254 x 10^{-3}	-2.4876
4	72.0	2.812 x 10^{-3}	-2.5510
5	108.0	2.104 x 10^{-3}	-2.6770
6	144.0	1.711 x 10^{-3}	-2.7668

k_2 = 6.32 x 10^{-4} ± 2.46 x 10^{-5} M.$^{-1}$ Sec.$^{-1}$
= 6.32 ± 0.25 x 10^{-4}

Table II-12. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 39.65°. A_o=1.218 x 10^{-1} M., B_o=5.035 x 10^{-3} M. Pseudounimolecular reaction.

#	Time 10^2 Sec.	Conc. NaOH B, M.	log B
1	18.0	4.523 x 10^{-3}	-2.3446
2	36.0	3.825 x 10^{-3}	-2.4173
3	54.0	3.225 x 10^{-3}	-2.4914
4	72.0	2.792 x 10^{-3}	-2.5541
5	109.0	2.124 x 10^{-3}	-2.6729
6	144.0	1.711 x 10^{-3}	-2.7668

k_2 = 6.325 x 10^{-4} ± 2.59 x 10^{-5} M.$^{-1}$ Sec.$^{-1}$
= 6.33 ± 0.26 * 10^{-4} M.$^{-1}$ Sec.$^{-1}$

Table II-13. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 60°. A_o=1.218 x 10^{-1} M., B_o=5.035 x 10^{-3} M. Pseudounimolecular reaction.

#	Time min.	Conc. NaOH B, M.	log B
1	8.0	4.333 x 10^{-3}	-2.3632
2	16.0	3.560 x 10^{-3}	-2.4486
3	24.45	2.905 x 10^{-3}	-2.5369
4	32.0	2.572 x 10^{-3}	-2.5898
5	48.0	1.966 x 10^{-3}	-2.7054
6	64.0	1.575 x 10^{-3}	-2.8027

k_2 = 2.44 x 10^{-3} ± 1.42 x 10^{-4} M.$^{-1}$ Sec.$^{-1}$
= 2.44 ± 0.14 x 10^{-3} M.$^{-1}$ Sec.$^{-1}$

Table II-14. Alkaline Hydrolysis of 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11) at 60°. A_o=1.218 x 10^{-1} M., B_o=5.035 x 10^{-3} M. Pseudounimolecular reaction.

#	Time min.	Conc. NaOH B, M.	log B
1	8.0	4.196 x 10^{-3}	-2.3772
2	16.0	3.531 x 10^{-3}	-2.4521
3	24.0	3.002 x 10^{-3}	-2.5226
4	32.0	2.562 x 10^{-3}	-2.5915
5	48.0	2.015 x 10^{-3}	-2.6957
6	64.0	1.614 x 10^{-3}	-2.7921

k_2 = 2.32 x 10^{-3} $\pm$ 1.1 x 10^{-4} M.$^{-1}$ Sec.$^{-1}$

k_2 = 2.32 $\pm$ 0.11 x 10^{-3} M.$^{-1}$ Sec.$^{-1}$

Table II-15. Activation parameters for 1-methoxy-2,2,3,4-tetramethyl-phosphetane 1-oxide (11).

Temp. °c.	25.1°	39.65°	60°
k_2, M.$^{-1}$ Sec.$^{-1}$	1.94 x 10^{-4}	6.32 x 10^{-4}	2.44 x 10^{-3}
	1.98 x 10^{-4}	6.32 x 10^{-4}	2.32 x 10^{-3}

$H^{\ddagger}$ = 13.32 $\pm$ 0.2 kcal

$S^{\ddagger}$ = -30.7 $\pm$ 1.2 cal.

Plot of $\log(k_2/T)$ vs $1/T$ for the alkaline hydrolysis of 1-methoxy-2, 2, 3, 4-tetramethylphosphetane 1-oxide (11) in water.

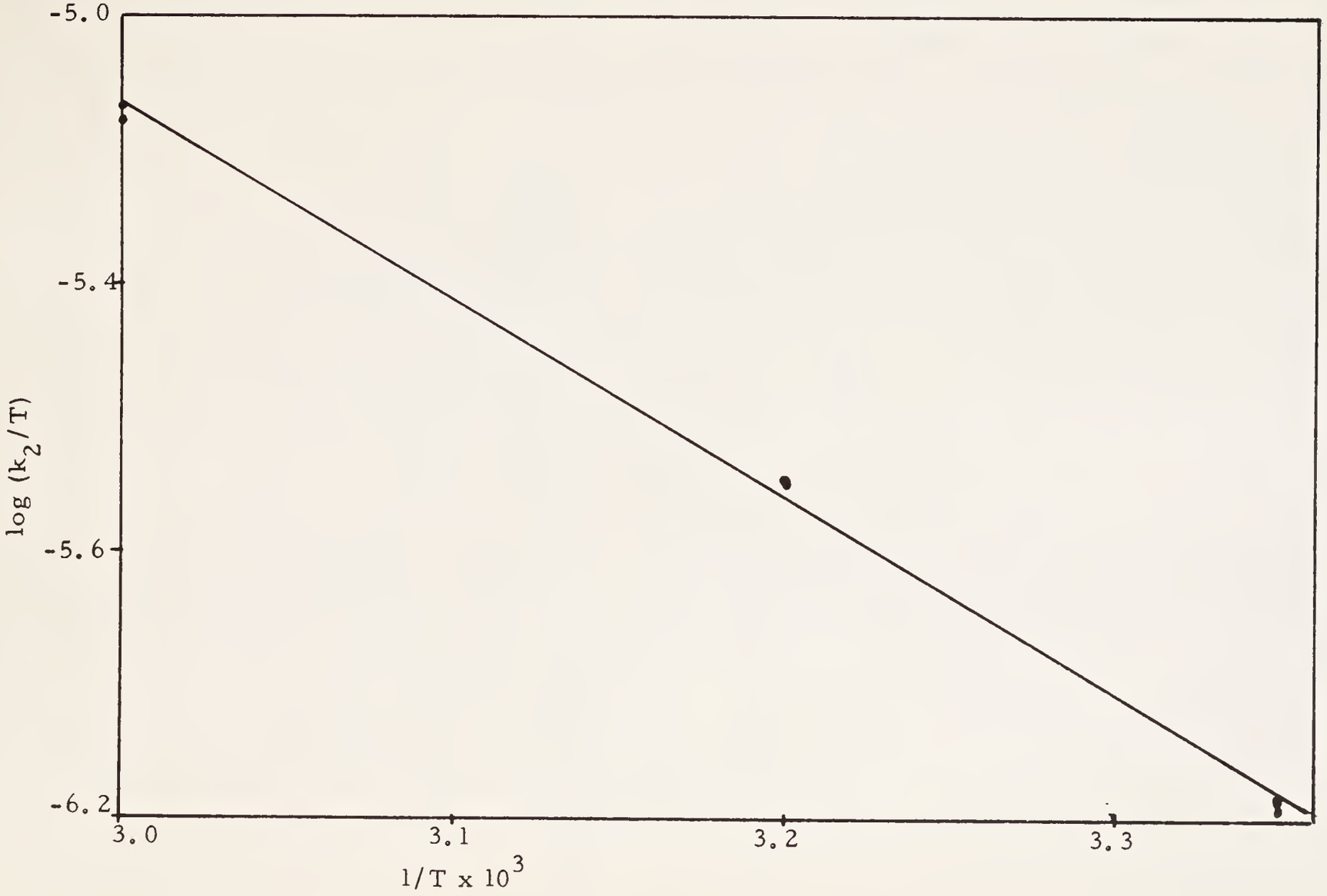


Fig. II-10

Table II-16. Alkaline of 1-methoxy-2,2,3,4,4-pentamethylphosphetane 1-oxide (86) at 25°.

Time hr.	B Conc. NaOH	log B_oA/A_oB
1.5	2.103×10^{-2}	0.0037
8.5	2.028	0.0097
24.0	1.794	0.0303
30.0	1.742	0.0355
48.5	1.539	0.0582
57.5	1.474	0.0666
77.5	1.322	0.0883
103.2	1.128	0.1225
144.0	9.545×10^{-3}	0.1614
192.0	7.804	0.2122

$A_o = 3.355 \times 10^{-2}$

$B_o = 2.158 \times 10^{-2}$

$k_2 = 5.88 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$.

$5.88 \pm 0.069 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$

Table II-17. Alkaline Hydrolysis of 1-methoxy-2,2,3,4,4-pentamethylphosphetane 1-oxide (86) at 25°.

Time hr.	Conc. NaOH B	log B_oA/A_oB
24.0	1.629×10^{-2}	0.0203
96.0	1.246	0.0561
120.0	1.177	0.0649
192.0	8.92×10^{-3}	0.1106
240.0	7.460	0.1446
312.0	6.330	0.1786

$A_o = 0.258$ M

$B_o = 0.01946$ M

$k_2 = 5.72 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$

$\pm 2.01 \times 10^{-6}$

$k_2 = 5.72 \pm 0.20 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$

Table II-17. Alkaline Hydrolysis of 1-methoxy-2,2,3,4,4-pentamethyl-phosphetane 1-oxide (86) at 25°.

time hr.	Conc. NaOH B.	Log B_oA/A_oB
24.0	1.629×10^{-2}	0.0203
96.0	1.246 x	0.0561
120.0	1.177	0.0649
192.0	8.920×10^{-3}	0.1106
240.0	7.460 x	0.1446
312.0	6.330	0.1786

$A_o = 0.0258$ M

$B_o = 0.01946$ M

$k_2 = 5.72 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$.

$\pm 2.01 \times 10^{-6}$

$k_2 = 5.72 \pm 0.20 \times 10^{-5}$ M.$^{-1}$ Sec.$^{-1}$

Table II-19. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 0°, by conductivity.

Time Sec.	R ohms	$-R(R_\infty - R)$
100	150	0.3797
250	166	0.4380
500	182	0.5014
750	196	0.5616
1000	207	0.6124
1500	228	0.7192
2000	246	0.8227
2500	267	0.9604
3000	280	1.0566
3500	298	1.2065
4000	307	1.2900
5000	329	1.5230
6000	349	1.7810
∞	545	

$A_o = B_o$ 2.00 10^{-2} M.

$k_2 = 3.10 \times 10^{-2}$ M.$^{-1}$ Sec.$^{-1}$ $\pm$ 2.79 x 10^{-4}

$k_2 = 3.10 \pm 0.028 \times 10^{-2}$ M.$^{-1}$ Sec.$^{-1}$

Table II-20. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 15°, by conductivity.

Time Sec.	Resistance R ohms.	$-R/(R_\infty - R)$
100	122	0.4729
200	135	0.5510
300	145	0.6170
400	153	0.6740
500	161	0.7352
600	167	0.7840
700	173	0.8357
800	180	0.9000
1000	194	0.9588
1250	205	1.1714
1500	218	1.3457
2000	238	1.6760
2500	252	1.9687
3000	262	2.2203
3500	274	2.5894
4000	281	2.8383
4500	291	3.2697
5000	297	3.5783
∞	380	

$A_o = B_o$ 0.02 M.

$k_2 = 9.05 \times 10^{-2}$ M.$^{-1}$ Sec.$^{-1}$.

$\pm 8.24 \times 10^{-4}$

$7.05 \pm 0.82 \times 10^{-2}$ M.$^{-1}$ Sec.$^{-1}$

Table II-21. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) in water at 15°. $A_o = B_o =$ 0.02 M.

Time Sec.	Resistance ohms	$-R/(R_\infty - R)$
100	124	.4844
200	133	.5385
300	143	.6034
400	152	.6667
500	157	.7040
620	167	.7840
700	174	.8447
800	179	.8905
1000	192	1.0213
1200	202	1.1348
1400	213	1.2754
1600	222	1.4051
2000	237	1.6573
2400	247	1.8571
2800	259	2.1405
3600	277	2.6893
4200	286	3.0426
∞	380	

$k_2 = 9.09 \times 10^{-2} \pm 6.13 \times 10^{-4}$ M.$^{-1}$ Sec.$^{-1}$

$9.09 \pm 0.061 \times 10^{-2}$ M.$^{-1}$ Sec.$^{-1}$

Table II-22. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 25.1°, by conductivity.

Time Sec.	Resistance R ohms	$-R/(R_\infty - R)$
75	108	0.5714
125	115	0.6319
175	121	0.6875
2225	129	0.7679
300	137	0.8563
400	147	0.9800
500	156	1.1064
600	161	1.1838
800	179	1.5169
1000	189	1.7500
1200	199	2.0306
1500	210	2.4138
2000	223	3.0135
2500	235	3.7903
∞	297	

$A_o = B_o$ 0.02 M

$k_2 = 1.44 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

$\pm 1.2 \times 10^{-3}$

$1.44 \pm 0.012 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

Table II-23. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 25.1°, by conductivity.

Time Sec.	Resistance R ohms	$-R/(R_\infty - R)$
100	193	0.5288
220	205	0.5989
300	220	0.6509
400	232	0.7117
500	2422	0.7658
600	256	0.8477
800	275	0.9717
1000	291	1.0899
1400	322	1.3644
1700	340	1.5569
∞	558	

$A_o = B_o = 0.01$ M. $k_2 = 1.58 \pm 0.012 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

Table II-24. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 33.9° , by conductivity.

Time Sec.	Resistance R ohms	$-R/(R_\infty - R)$
100	174	0.6237
150	181	0.6654
200	191	0.7290
300	205	0.8266
400	220	0.9442
500	232	1.0498
600	244	1.1675
700	263	
800	263	1.3842
1000	281	1.6337
1500	312	2.2128
2000	335	2.8390
2500	351	3.4412
3000	366	4.2070
∞	453	

$A_o = B_o = 0.01$ M

$k_2 = 2.68 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$ $\pm 3.35 \times 10^{-3}$

$268 \pm 0.034 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

Table II-25. Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethyl-phosphetane 1-oxide (15) at 33.9° , by conductivity.

Time Sec.	Resistance R ohms	$-R/(R_\infty - R)$
100	172	0.6078
150	181	0.6606
200	190	0.7170
250	197	0.7636
300	203	0.8056
400	219	0.9280
500	232	1.0404
600	243	1.1462
700	254	1.2637
800	262	1.3575
1000	281	1.6149
1500	314	2.2270
2000	334	2.7603
2500	351	3.3750
3000	366	4.1124
∞	455	

$A_o = B_o = 0.01$ M

$k_2 = 2.64 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

$\pm 2.74 \times 10^{-3}$

$2.64 \pm 0.027 \times 10^{-1}$ M.$^{-1}$ Sec.$^{-1}$

Table II-26. Activation Parameters for Alkaline Hydrolysis of 1-methoxy-2,2,3,3-tetramethylphosphetane 1-oxide (15) in water.

Temperature OK	k_2 M.$^{-1}$ Sec.$^{-1}$	$\Delta H^{\ddagger}$ kcal/M	$\Delta S^{\ddagger}$ e.u.
273.1	3.10×10^{-2}		
273.1	3.31×10^{-2}		
288.1	9.05×10^{-2}	9.63±0.36	-29.9±1.30
288.1	9.09×10^{-2}		
298.2	1.44×10^{-1}		
298.2	1.42×10^{-1}		
307.0	2.68×10^{-1}		
307.0	2.64×10^{-1}		

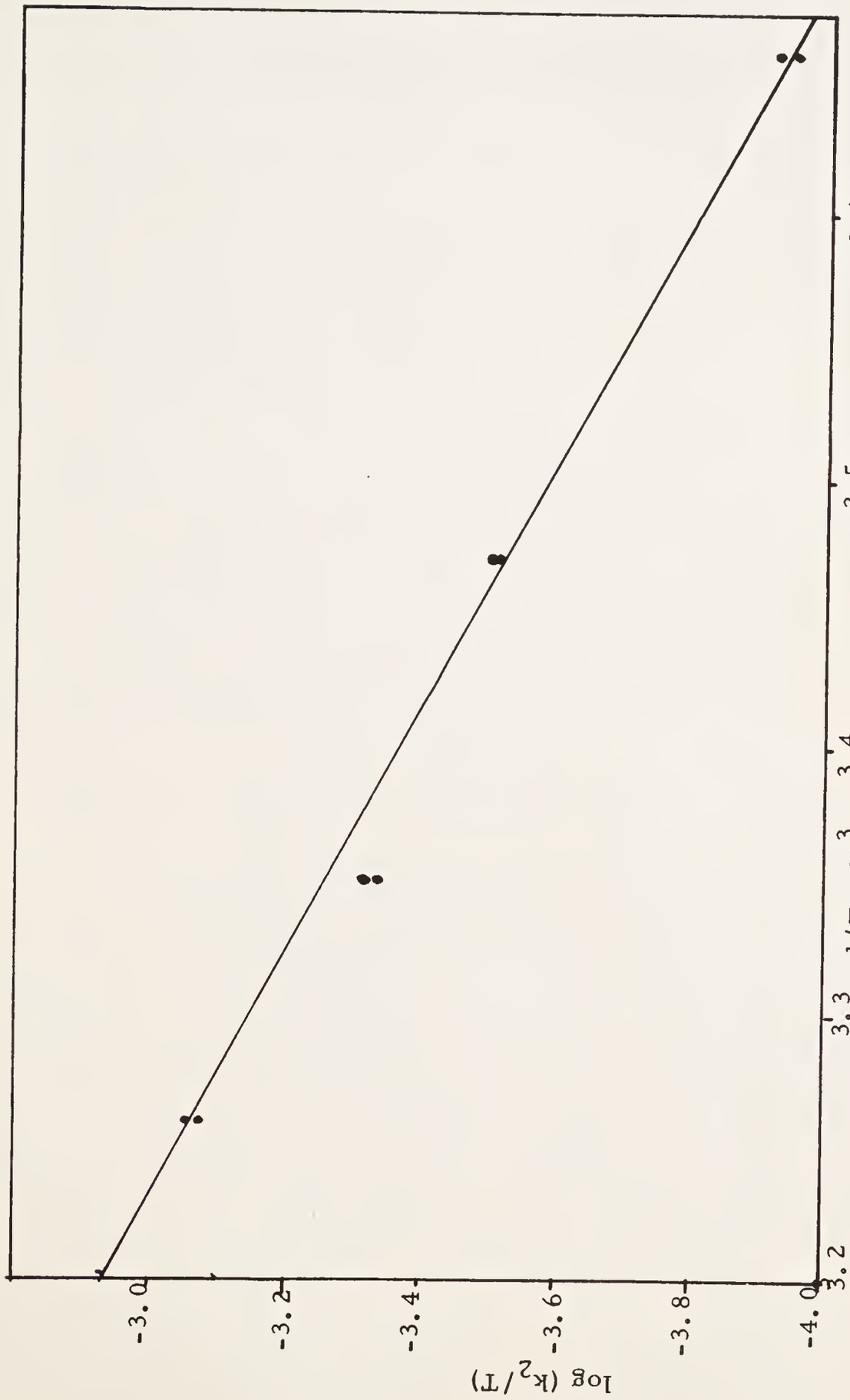


Fig. II-11. Plot of log (k_2/T) vs 1/T for the alkaline hydrolysis of 1-methoxy-2, 2, 3, 3-tetramethylphosphetane 1-oxide (15) in water.

3. Hydrolysis of Phosphonium Salts

a. Background. Hoffmann [90] first studied the thermal decomposition of quaternary ammonium hydroxide. He observed that tetramethylammonium hydroxide yields trimethylamine and methanol on heating:

$$(CH_3)_4 N^+ OH^- \xrightarrow{\Delta} (CH_3)_3N + CH_3OH$$

However, if one of the alkyl groups in the salt possesses a B-hydrogen atom, the products of the reaction are a tertiary amine, an alkene and water [91]:

$$(C_2H_5)_3\overset{+}{N}\text{-}CH_2\text{-}CH_3 + OH^- \xrightarrow{\Delta} (C_2H_5)_3N + CH_2{=}CH_2 + H_2O$$

An extensive study by Hoffman on the B-elimination led to the well-known Hoffmann degradation which is so widely used in organic chemistry[92].

In contrast to the ammonium hydroxides, tetraethylphosphonium hydroxide thermally decomposes to yield triethylphosphine oxide and ethane[93]:

$$(C_2H_5)_4\overset{+}{P} + OH^- \xrightarrow{\Delta} (C_2H_5)_3P{=}O + C_2H_6$$

The generality of the reaction was established by Hoffman.

Letts and co-workers [94] found that the decomposition of tetrabenzylphosphonium hydroxide could be carried out at comparatively low temperature to yield tribenzylphosphine oxide and toluene. Meisenheimer [95] and Ingold [96] studied the reaction in detail with variously substituted phosphonium salts and observed that the ease of elimination of substituents parallels the stability of the corresponding anion. The following order of decreasing ease of elimination of substituents was observed:

benzyl> phenyl> methyl> β-phenethyl> ethyl> higher alkyls

The study of this preferential elimination of groups was the basis of the

isolation of an asymmetric phosphine oxide [97]:

$$(PhCH_2)_4\overset{+}{P} \xrightarrow{OH^-} (PhCH_2)_3P{=}O \xrightarrow[ii)\ RI]{i)\ Red\ n} (PhCH_2)_3\overset{+}{P}R \xrightarrow{OH^-}$$

$$(PhCH_2)_2\overset{O}{\overset{\|}{P}}R^- \xrightarrow[ii)\ RI]{i)\ Red\ n} (PhCH_2)_2\overset{+}{P}R\ R'\ I^- \xrightarrow{OH^-} PhCH_2\overset{O}{\overset{\|}{P}}\begin{matrix}R\\ \diagdown\\ \diagup\\ R'\end{matrix}$$

The foregoing does not imply that the olefin formation or similar reactions analogus to those in ammonium salts are unknown in phosphonium salts. Hey and Ingold [98] have shown that elimination of an alkene could be a predominant pathway for the decomposition of phosphonium salts with proper substituents:

$$\begin{matrix}Ph\\ \diagdown\\ CH - CH_2\overset{+}{P}(\underline{n}Bu)_3\\ \diagup\\ Ph\end{matrix} \xrightarrow{OH^-} Ph_2C = CH_2 + (\underline{n}Bu)_3P + H_2O$$

Analogous elimination of the phosphine moiety as the major reaction has also been observed in the following cases described by Horner and Hoffmann [99]:

$$\overset{+}{P}(CH_2OH)_4 + OH^- \longrightarrow P(CH_2OH)_3 + CH_2O + H_2O$$

$$\overset{+}{P}(CH_2Cl)_4 + OH^- \longrightarrow P(CH_2Cl)_3 + CH_2O + HCl$$

It might be expected that the yield of the olefin could be increased by using a stronger base such as ethoxide ion. Hey and Ingold[98] studied the decomposition of quaternary phosphonium ethoxide. They observed that only a small increase in the yield of olefin was obtained in the compounds with favorable structure. The predominant path was the formation of an alkane.

Thus, the alkaline decomposition of phosphonium salts generally leads

to a phosphine oxide and a hydrocarbon. A systematic investigation of this reaction has been reported recently [96,100]. McEwen and co-workers[100] measured the kinetics of the base catalyzed decomposition of benzylethymethylphenylphosphonium chloride in aqueous sodium hydroxide solution: They observed that the reaction was third-order overall, first-order in the concentration of the phosphonium salt and second-order in the hydroxide ion concentration i.e.,

$$\text{Rate} = k_3^* [P^+] [OH^-]^2$$

Alkaline decomposition of a series of meta and para substituted benzyltribenzylphosphonium halides in water-1,2-dimethoxyethane solution were studied by McEwen and co-workers[101,102]. In addition to the observation that all phosphonium salt decomposition reactions were third-order, the following conclusions were drawn:

i. the relative ease of elimination of various benzyl groups parallell their stability as anions,

ii. the relative ease of elimination of a group is influenced by the nature of the non-departing groups,

iii. a good correlation with values in an application of the Hammett equation was obtained.

Hey and Ingold [98] had arrived at almost the same conclusions except that the dependence of the rate on the non-departing group was not recognized.

On the basis of the above data, McEwen and co-workers[102] proposed the following step-wise mechanism:

$$R_4\overset{+}{P} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_4P{-}OH$$

$$R_4P\text{-}OH + OH^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R_4P\text{-}\bar{O} + H_2O$$

$$R_4P\text{-}\bar{O} \xrightarrow{k_3} R_4P = O + R^{\ominus}$$

$$R^- + H_2O \xrightarrow{f} RH + OH^-$$

A steady state approximation, assuming the rate of change of the concentration of intermediates $[R_4POH]$ and $[R_4P\text{-}\bar{O}]$ to be zero leads to the following expression:

$$-\frac{d[P^+]}{dt} = k_1 [P^+] [OH^-] \left[\frac{k_2 k_3 [OH^-]}{k_{-1}(k_{-2} + k_3) + k_2 k_3 [OH^-]} \right]$$

For the reaction to be third-order the following condition must be observed:

$$k_2 k_3 [OH^-] \ll k_{-1}(k_{-2} + k_3)$$

Steps 2 and 3 may be discrete or concerted.

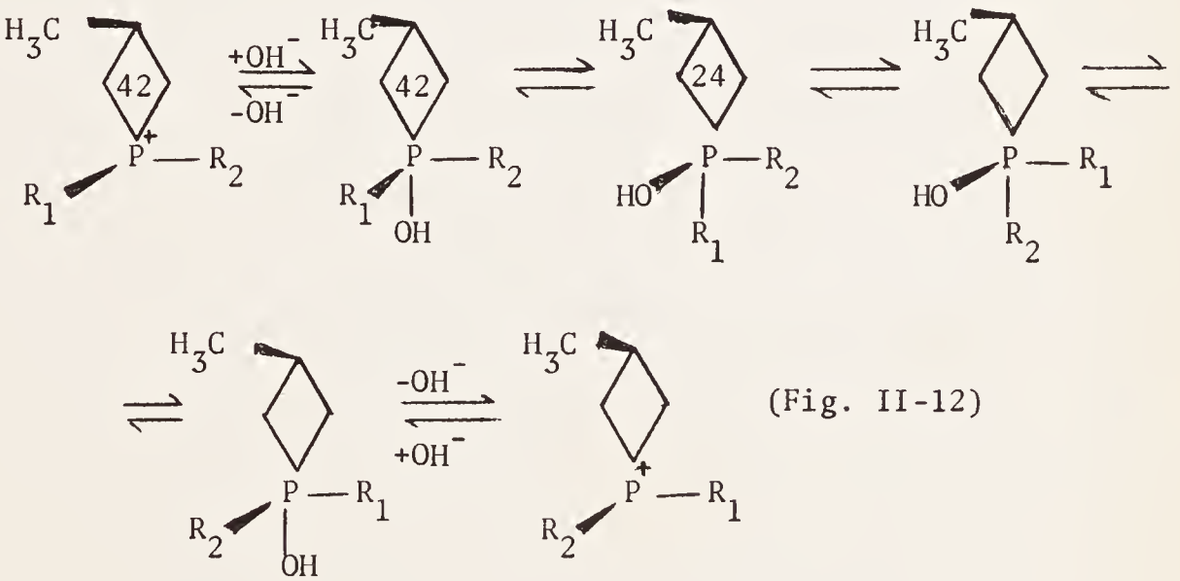
b. Result and Discussion. The step-wise mechanism postulated above includes the formation of intermediates in the equilibrium process. This is contrary to the original assumption by Ingold [98]. He assumed the reaction to be second-order overall, in which the attack of hydroxide ion was the rate determining step. The equilibrium step can be easily tested in a system in which pseudorotation of the intermediate phosphorane followed by reversal of the new intermediate would lead to isomerization of the starting material. As yet, there have been no reports in which such a

racemization of the starting material has been shown to occur. This has been mainly due to the fact that the intermediates in such cases probably have a high energy barrier for pseudorotation. The phosphetanium salts are unique for two reasons:

i) due to the strain in the ring, the formation of the intermediate should be facilitated,

ii) pseudorotation of a properly substituted phosphorane intermediate may involve low energy barriers.

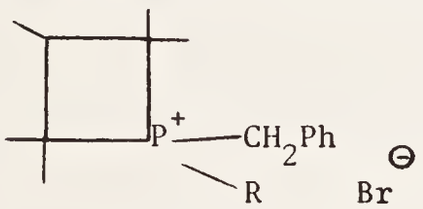
The scheme in fig. 12 represents the minimum number of different isomeric phosphoranes the system would have to go through, in order to change from the trans to the cis isomer of a hypothetical phosphetanium salt and vice versa:



Thus, a minimum of three pseudorotations and four intermediate phosphoranes are required to change the configuration of the system from trans to cis and reverse.

It is conceivable therefore, that the cis isomer of a phospetanium salt can be converted to the trans isomer. This possibility of isomer interconversion can be verified very conveniently by nmr spectroscopy.

The chemical shift of at least one of the groups in the compounds investigated was sufficiently different to demonstrate that interconversion did (or did not) occur. Various isomeric compositions (9:1), (1:1) (1:4) of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in deuteriochloroform were treated with one drop of 1N sodium hydroxide solution. An almost instantaneous change occured to give a fianl composition of 1:4. The results of this and other compounds investigated under similar conditions are given in table 27.



(94); R=Ph a, R,CH_3 trans

(24); R=CH_3 b, R,CH_3 cis

However, contrary to these results are the observations of Trippett[103]. He has claimed that (94a) and (24a) each yield a mixture of isomeric oxides on treatment with base. Quenching of the corresponding ylid reaction with n-buytllithium was shown to give a mixture of isomeric phosphetanium salts in each case; as would be expected on the basis of the equilibration of salts. However, Trippett reported that alkaline decomposition of salts (94b) and (24b) each yielded a predominance of only one isomeric oxide. This led him to suggest that an isomer cross-over in (94a) and (24a) occurred through a ylid intermediate which was proposed to go through an sp^2d planar transition state in order to yield the isomeric ylid. The latter would abstract a proton from the solvent to give the isomeric phosphetanium salt. He argued that the formation of the proposed planar transition state was facilitated due to the interaction between the 2-methyl group and the anionic substituent at the phosphorus in the ylid in (94a) and (24a) only. The mechanism above would be expected to lead to a complete conversion of both (94a) and (24a) to (94b) and (24b), respectively. This

hypothesis can be easily disproved because the same equilibrium is reached starting with either isomer of the salt (table 27). Furthermore, it was found that 1-phenyl-1,2,2,3,4,4-hexamethylphosphetanium bromide (27) on treatment with sodium deuterioxide in D_2O underwent an isomer interconversion faster than the deuterium exchange. If the isomer interchange occurred through an ylid intermediate, the rate of deuterium exchange would be expected to be faster or equal to the rate of isomer corss-over. The planar transition state proposed by Trippett [103] would also be anticipated to be highly strained. It should be pointed out here, however, that the conditions of Trippett's experiments and those of this investigation were not identical.

Another interesting feature of the phosphetanium salts is the formation of predominantly one isomer of the phosphetane oxide during the alkaline decomposition of the corresponding benzyl salts. Thus, various mixtures (9:1, 1:1, 1:4) of the cis and trans isomers of (94) when treated with alkaline sodium hydroxide give a predominance (1:9) of one isomeric phosphetane oxide (20) (cis:trans)[104]. Similarly, treatment of either pure isomer of (24) with alkali gives rise to an 85:15 mixture of oxide (22) with the same isomer of the oxide predominating in each case. The rationale for this observation may be analogous to the one proposed for the predominant formation of one isomer of acid chloride (5). Thus, an addition of a molecule of base to the cis phosphetanium salt leads to intermediate (95) (fig. 11), whereas phosphorane (96) is produced from the trans salt. Pseudorotation of these intermediate leads to other trigonal-bipyramidal structures. However, during the decomposition, the steric interaction of the solvated hydroxyl group with the methyl group at position 3, leads to a faster decomposition of this intermediate (98) than that of (97), i.e., $k' << k''$(fig. 11).

Table II-27. Equilibration of Phosphetanium Salts with Base.

Compound	Solvent	Composition (trans:cis) (*) Initial	Final
(94)	$DCCl_3$	9:1,1:1	1:4
(94)	H_2O	9:1,1:1	1:2.5
(24)	$DCCl_3$	95:5,5:95	1:2
(24)	H_2O	95:5,5:95	1:2
(27)	H_2O	95:5	1:2.5
(18)	$DCCl_3$	28:1	3.4:1
(27)	D_2O	8.7:1	1.5:1 (D-exchange 15%)

(*) Cis and trans relationship for the substituent at phosphorus with respect to 3-methyl.

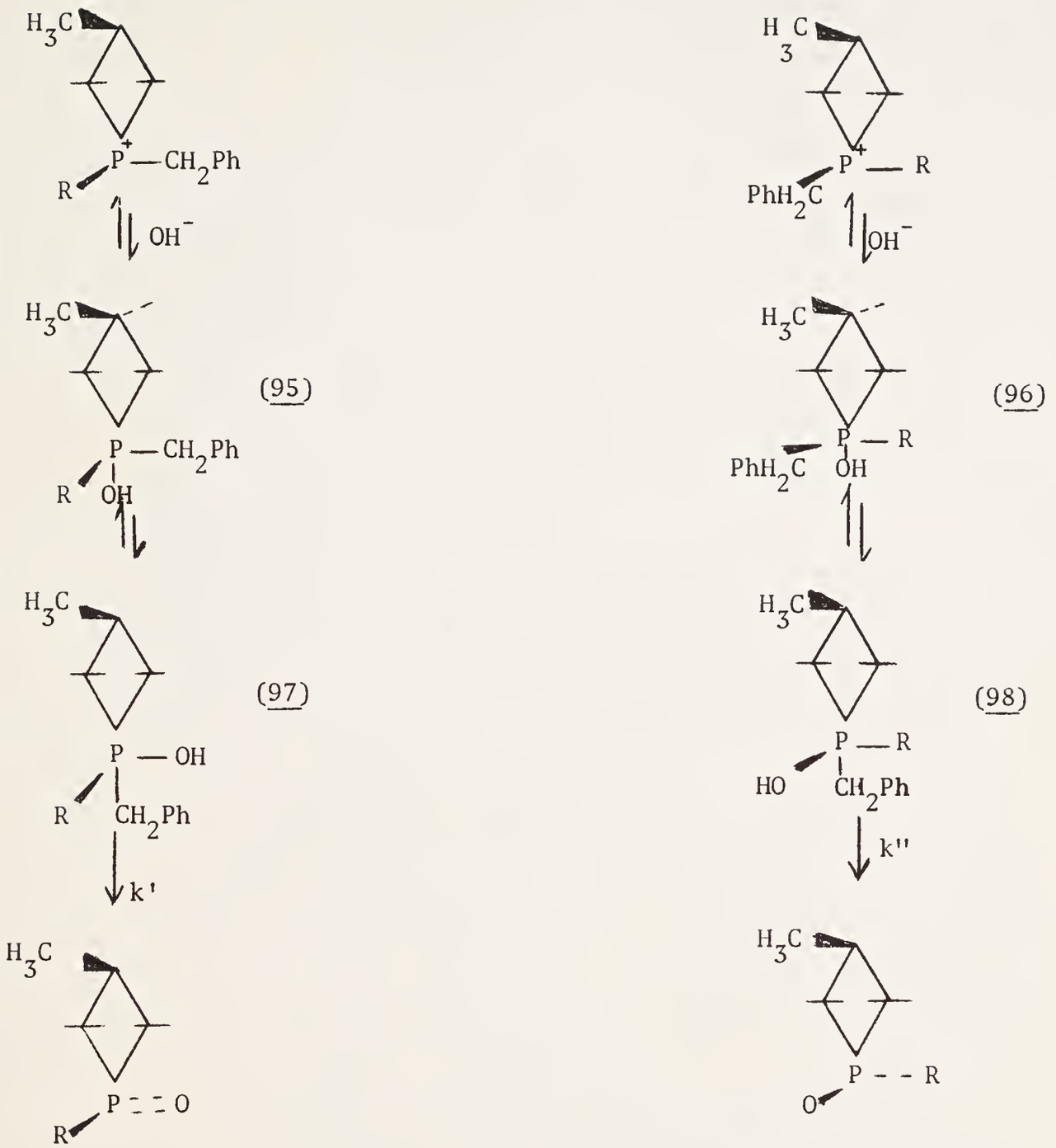
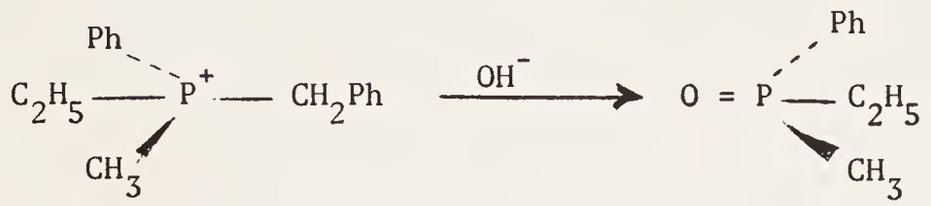

H3C
P+—CH2Ph
R
OH−
(95)
P—CH2Ph
R OH
(96)
PhH2C
(97)
P—OH
CH2Ph
k'
(98)
HO
k''
P=O
P--R
O

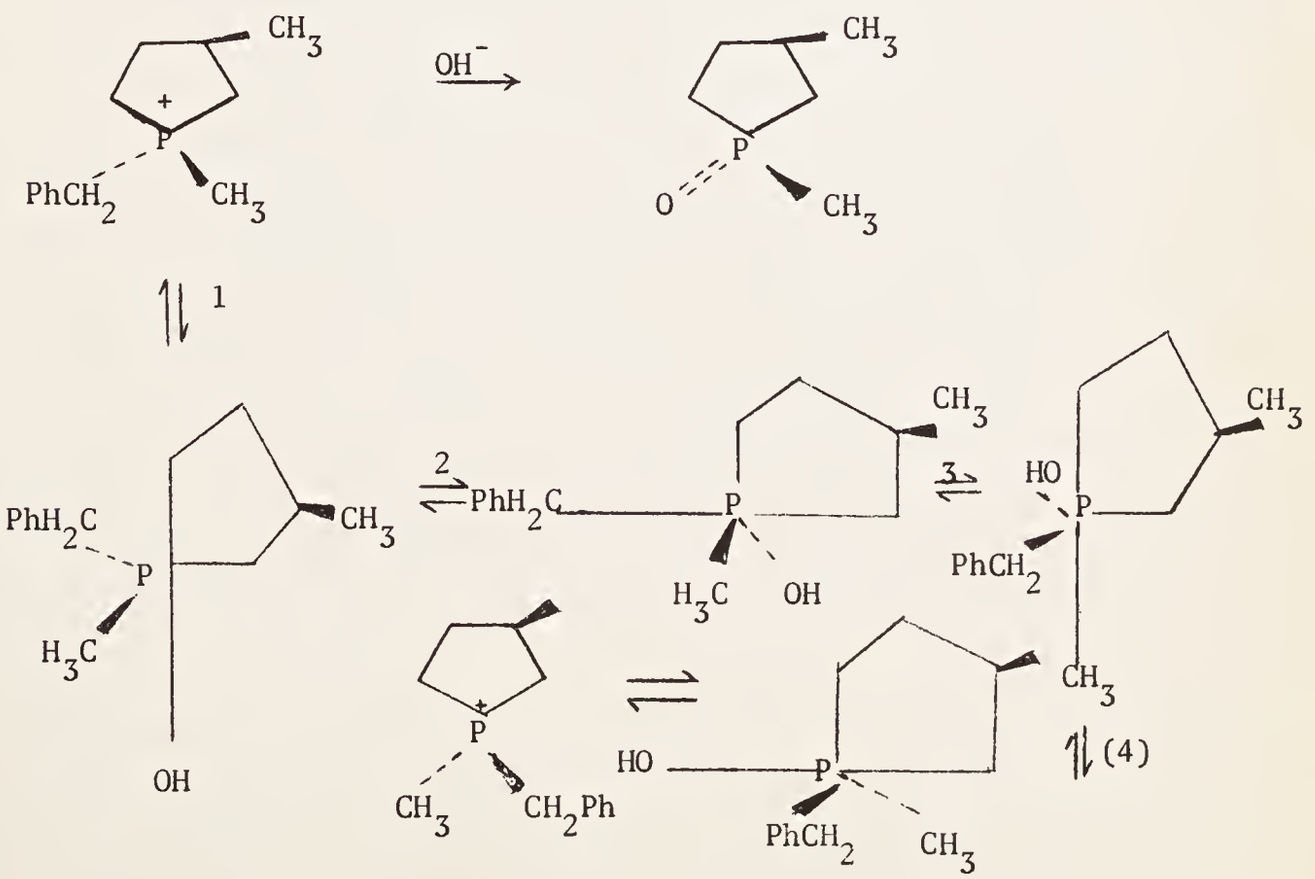
Fig. II-13.

In view of the above discussion, the alkaline decomposition of optically active benzylethylmethylphenylphosphonium iodine to give the phosphine oxide with inverted configuration [100] appears contradictory:



This, however, can be easily explained by the apparent lack of pseudorotation in the intermediate phosphorane, since pseudorotation would probably be energetically unfavorable.

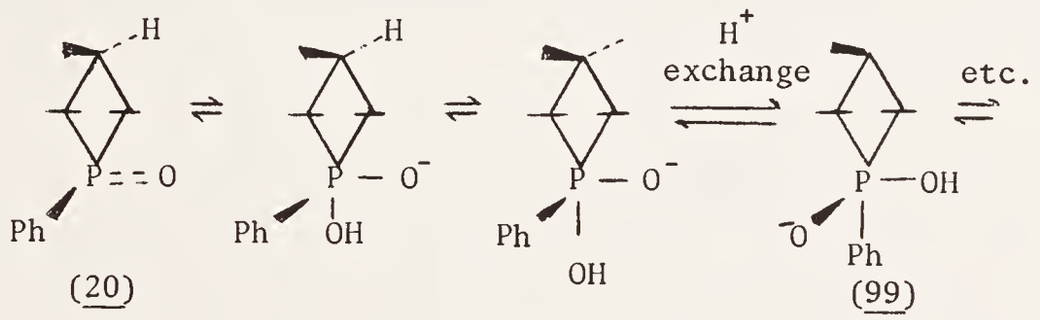
In this context, the results of Marsi [106] are very interesting. An alkaline decomposition of each isomer (cis and trans) of 1,3-dimethyl-1-benzylphospholanium salt led to the oxide with retention of configuration:



Trippett [103] has recently reported the formation of a different isomeric composition of oxides (20) and (22) starting with the different isomers of the corresponding benzyl salts (94) and (24), respectively. The results are inconsistent with the observation of equilibration of salts which would necessarily lead to the same ratio of isomeric oxides, regardless of the stereochemistry of the starting salt. Marsi proposed that the attacking hydroxide ion enters from the apical position; but that the benzyl anion departs from an equatorial position. Although, this assumption explains the retention mechanism it can be questioned on two grounds: the principle of microscopic reversibility [35] and the principle of least motion (see also page 67)[33,84] both of which require apical entry and apical departure. In order to interconvert the isomers in this case, the phosphorane intermediate initially produced, must go through a minimum of three pseudorotational steps. It appears therefore, that the five-membered ring is not as strained as the four-membered ring because the C-P-C ring angle in this case is 95° [68] compared to 83° [27] in the four-membered ring. As a result, the energy of placing an electon donating methyl group in the apical position may not be overcome by the relief of the strain achieved in going from the starting material to the intermediate. Thus, only one pseudorotation (e.g., step 2 or 4) occurs which leads to retention of configuration. It is equally probable that the molecule does not go through a pseudorotation as a discrete step but only as a part of a decomposition step in the transition state.

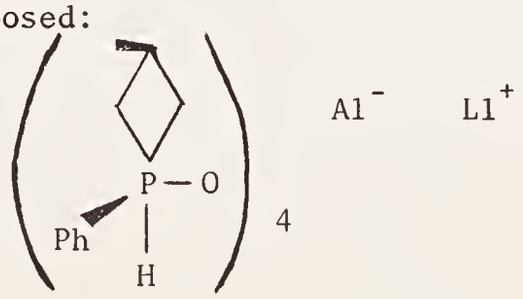
Similar to the interconversion of the isomeric salts, the isomer interchange of the oxides can also be brought about by base. In this case, however, refluxing of the oxide with 1N sodium hydroxide in 95% ethanol

is required [104]. The process is also complicated by the simultaneous production of the open-chain acids. Thus, pure (98%) cis 1-phenyl-2,2,3,4,4-pentamethylphosphetane oxide (20) was treated with alkali under the above conditions for 14 hr.. The unreacted oxide was a mixture of the trans and cis isomers in the ratio (22:78) respectively; as determined by nmr integration. The interconversion can take place through the pseudorotation of the phosphorane intermediate (see scheme belwo) which would result in a symmetrical intermediate (99) . Decomposition following a pseudorotation of (99) would give both isomers with equal probability. Since the phosphine oxide (20) does not have any ∝-protons, the necessity of a ylid intermediate can be easily ruled out [103] in this case.



(20) (99)

The isomerization of the oxide (20) can also be brought about by other reagents. Mislow and co-workers [107] have demonstrated recently that in the presence of lithium aluminum hydride, (20) undergos isomer cross-over. The following intermediate was proposed:

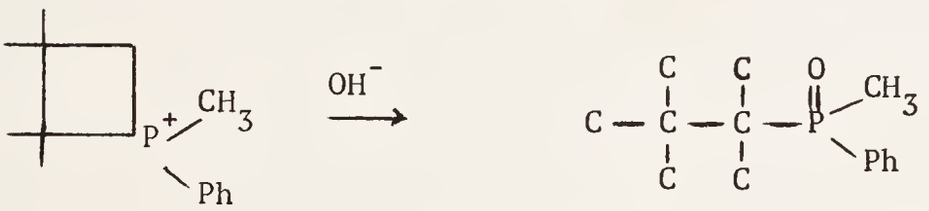


(the alkaline decomposition of the phosphonium salts) as shown earlier is third-order [100] and passes through a phosphorane intermediate. An investigation of the kinetics of the alkaline decomposition of the salts was undertaken with a two-fold purpose:

i) to ascertain whether the reactions follow third-order kinetics,

ii) and to obtain the magnitude of the acceleration of the rate, produced on formation of a relatively strain free intermediate.

The available phosphetanium salts provuded an interesting set of substrates. Thus, exocyclic cleavage of the benzyl group could be studied in compounds (24), (26), (94), (100), (101). Compounds (27) and (102) were selected in order to investigate the rates of ring opening and ring expansion reaction, respectively, Chorvat [2] showed that compound (102) is hydrolyed by base to yield open-chain compound (103):



(102) (103)

Compound (27) on the other hand, was shown to undergo ring expansion to yield (29a) (see p.11). The rate of the alkaline hydrolysis of (104) was also examined in order to provide a comparison of the phosphetanium salts with open-chain systems. Table 28 shows the rates of different compounds in 50% ethanol-water at 25°.

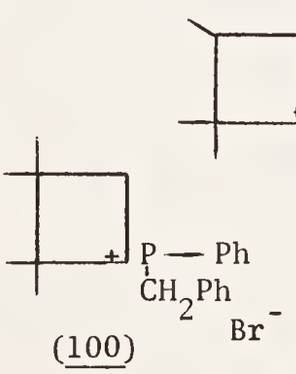
An inspection of table 28 reveals that compounds (26) and (24) hydrolyzed (60) and 15 times faster than is triphenylbenzylphosphonium bromide (105). The latter is substituted with three electron withdrawing phenyl groups and would be expected to be hydrolyzed much faster than its alkyl analog. Thus, the ease of intermediate formation in the cyclic compounds is reflected in their rates of hydrolysis.

The dramatic effect of the strain can be seen more clearly in the following comparison. Aksnes[108] has shown that the salt with a five-

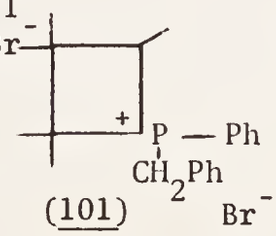
Table II-28. Alkaline Hydrolysis of Phosphonium Salts. Third-Order Rate Constants at 25° in 50% Ethanol-Water. Ionic Strength 0.1M.

Compound	k_3 ($M^{-2}Sec.^{-1}$)
(24)	$1.09\pm0.02 \times 10^{0}$
(26)	$4.43\pm0.08 \times 10^{0}$
(27)	$1.54\pm0.013 \times 10^{-1}$
(94)	$8.13\pm0.032 \times 10^{-1}$
(100)	$2.097\pm0.03 \times 10^{3}$
(101)	$1.37\pm0.023 \times 10^{2}$
(102)	$2.82\pm0.026 \times 10^{0}$
(104)	$1.29\pm0.018 \times 10^{-1}$
(105)	7.08×10^{-2} (ref. 109)

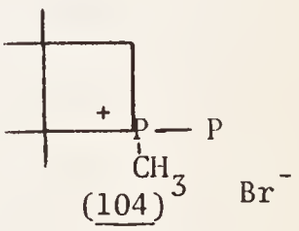
(24): $R_1=CH_3$, $R_2=CH_2Ph$
(26): $R_1=R_2=CH_2Ph$
(27): $R_1=CH_3$, $R_2=Ph$
(94): $R_1=CH_2Ph$, $R_2=Ph$



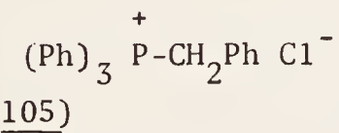
(100)



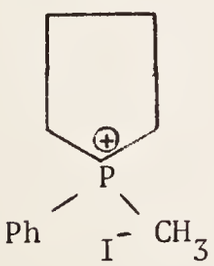
(101)



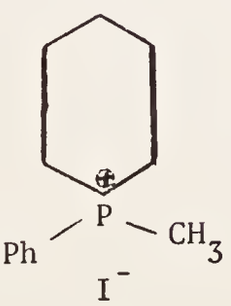
(104)



(105)



(107)



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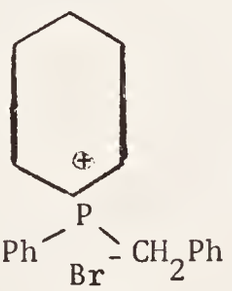

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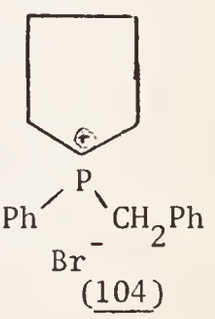
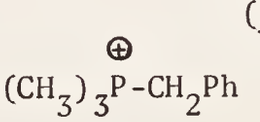


(104)



(109)

membered ring (107) is hydrolyzed 1300 times faster than the salt with a six-membered ring (108). Both of these salts have been shown to decompose with exclusive exocyclic cleavage. Salt (104) is known to undergo exclusive exocyclic cleavage as well. Based on the assumption that the same arguments would hold for compound (106), it would be reasonable to expect that (104) would also hydrolyze about 1300 times faster than (106). In table 28, compound (100) which decomposes 10^4 times faster than the five-membered ring, salt (104), should react $1300 \times 10^4 \approx 10^7$ times faster than (106). Since the latter rate is probably as fast as that of the open-chain system (109). The hypothesis, therefore that the strain in the phosphetanium salts is relieved in going to the trigonal-bipyramidal intermediate is corroborated.

A peculiar solvent effect is demonstrated in table 29. The reaction of the phosphonium salt with hydroxide ion involves the reaction between two oppositely charged species. In the following equation, a relation between the rate constant and the dielctric constant of the medium is given (109):

$$\ln k = \ln k'_o - \frac{NZ_a Z_b . e^2}{D\ R\ T\ r^*}$$

where k=calculated rate constant in a medium of infinite dielectric constant, N=Avogadro's number, Z_a and Z_b are the charges of the two ions, e=electron charge, D=dielectric constant, R=gas constant, T=absolute temperature and r*=distance between the ions in the activated complex. The equation predicts an increase in the rate of the reaction in a medium of lower dielectric constant for a reaction between two oppositely charged ions. Thus, the acceleration of the rate of hydrolysis in 50% ethanol-water is not unanticipated. However, the magnitude of the acceleration

is unexpectedly large and so the effect of the solvent may be more complex.

The activation parameters for one system (100) in aqueous solution are given in table 43. Unfortunately, the paucity of such data in other systems prevents a meaningful conclusion at the present time. Further, the activation parameters are overall values and hence, do not reflect on any individual step of the reaction.

Table II-29. Solvent Effect on the Hydrolysis of Phosphonium Salts Third-Order Rate Constants at 25°. Ionic Strength 0.1M.

Compound	Solvent	$k_3(M^{-2}Sec.^{-1})$	$\frac{k_3 \text{ (Ethanol-water)}}{k_3 \text{ (water)}}$
(94)	Water	6.80×10^{-2}	1200
(94)	50% ethanol-water	8.16×10^{1}	
(100)	Water	1.75×10^{1}	119.8
(100)	50% ethanol-water	2.10×10^{3}	
(101)	Water	7.70×10^{-1}	178.3
(101)	50% ethanol-water	1.37×10^{2}	

c. Experimental. The alkaline decomposition of phosphonium salts was determined, initially by titration methods. Separately prepared solutions of the phosphonium salt (0.005 N) and NaOH (0.005 N), both in 50% ethanol-water, were equilibrated in a double chambered flask. The solutions were mixed and a 5.0 ml aliquot of the mixture was quenched with 10 ml of 0.005 N HCl solution. The excess of the acid was titrated against a standard NaOH solution to determine the amount of unreacted alkali in the reaction mixture. The concentration of the phosphonium salt was calculated on the basis of the stoichiometry (1:1) since:

$$R_4\overset{+}{P} \; = \; 2OH^- \longrightarrow R_3P = O + R^- + H_2O \longrightarrow RH + OH^-$$

$$\therefore \quad R_4\overset{+}{P} \; + \; OH^- \longrightarrow \text{Products}$$

The results obtained for compounds (94) and (102) are tabulated (Tables 30-36) The ionic strength of the solution was not maintained constant in these runs [108]. A straight line was obtained by plotting $1/C^2$ vs time showing the reaction to be third-order. The reactions were followed to at least 60% completion. No correlation was obtained for a second-order reaction.

Similarly, in the case of compound (100), the third-order rate constants were determined in the presence of 0.2M KCl solution in water. The rate constants for three different temperatures were obtained which were subsequently used for computing the activation parameters.

After having ascertained that the reactions are third-order, the method of following the kinetics of these reactions was changed. According to the third-order equation:

$$\text{Rate} = k_3^* \; A \; B^2 \quad \text{where A = Conc of } \overset{+}{P} \text{ salt}$$

$$B = \text{Conc of NaOH}$$

If the concentration of the base is not allowed to change appreciably, the equation becomes:

$$\text{Rate: } = (k_3^* B^2)\ A = k_{obs} A$$

From the value of k_{obs} at different base concentration, k_3^* can be determined from the relation:

$$k_{obs} = k_3^* B^2$$

A pseudo first-order plot was obtained by following the decrease in the concentration of the phosphonium salt. This could be conveniently accomplished with the aid of uv spectrophotometer. In a separate experiment the wave length at which a maximum change in absorbance for a compound occurred, was determined. The need for the determination of extinction coefficient was obviated because of the independance of pseudo first-order reaction on the concentration of the species in question. A plot of log $(A_t - A_\infty)$ vs time where A_t is absorbance at time t and A_∞ that at time infinity; gave a straight line whose slope was equal to 1/2.303 x k_{obs}. Determination of k_{obs} was performed at various alkali concentration. The alkali solution was prepared from a standard stock solution; e.g., for the preparation of 0.1 N NaOH in 50% ehtanol-water solution: 10 ml of 1 N NaOH diluted with exactly 50 ml of absolute ethanol followed by diultion to exactly 100 ml with distilled water at 25°. To make the total ionic strength to 0.2 M, 0.58454 g of sodium chloride was dissolved in the solution prior to dilution.

Equal volumes of both the phosphonium salt solution and NaOH solution (containing the requisite amount of NaCl to make up the required ionic strength) were mixed after equilibrating them separately at 25° for at least 20 min.. The resultant solution had half the ionic strength and half the base concentration of the original base solution (In the example above,

the final Conc. NaOH = 0.05 N, ionic strength = 0.1 M.. The concentration of the phosphonium salt was kept to near 5 x 10^{-4} M (after mixing) so that its contribution to the ionic strength could be neglected. The uv determinations were performed on the double beam Cary 11 spectrophotometer with the cell compartment jacketted with and connected to tubes through which water at 25° was circulated. No reference was used except for the initial setting of the instrument in which case matched cells containing the solvent of the reaction was used. The sweep was performed at a fixed wave length by running the chart at a known constant speed. The reading at time =∞ was taken after about 10 half lives for each reaction. An exponential plot fo the change in absorbance vs time thus obtained from the plot was utilized for computing the values of $\log(A_t - A_\infty)$. The k_{obs} was determined by using a least-squares program designed for Wang 300 electronic calculator (except where indicated in which case a graphical determination of k_{obs} was made). The third-order rate constants were similarly computed from the one parameter least-squares operations on k_{obs} vs B^2.

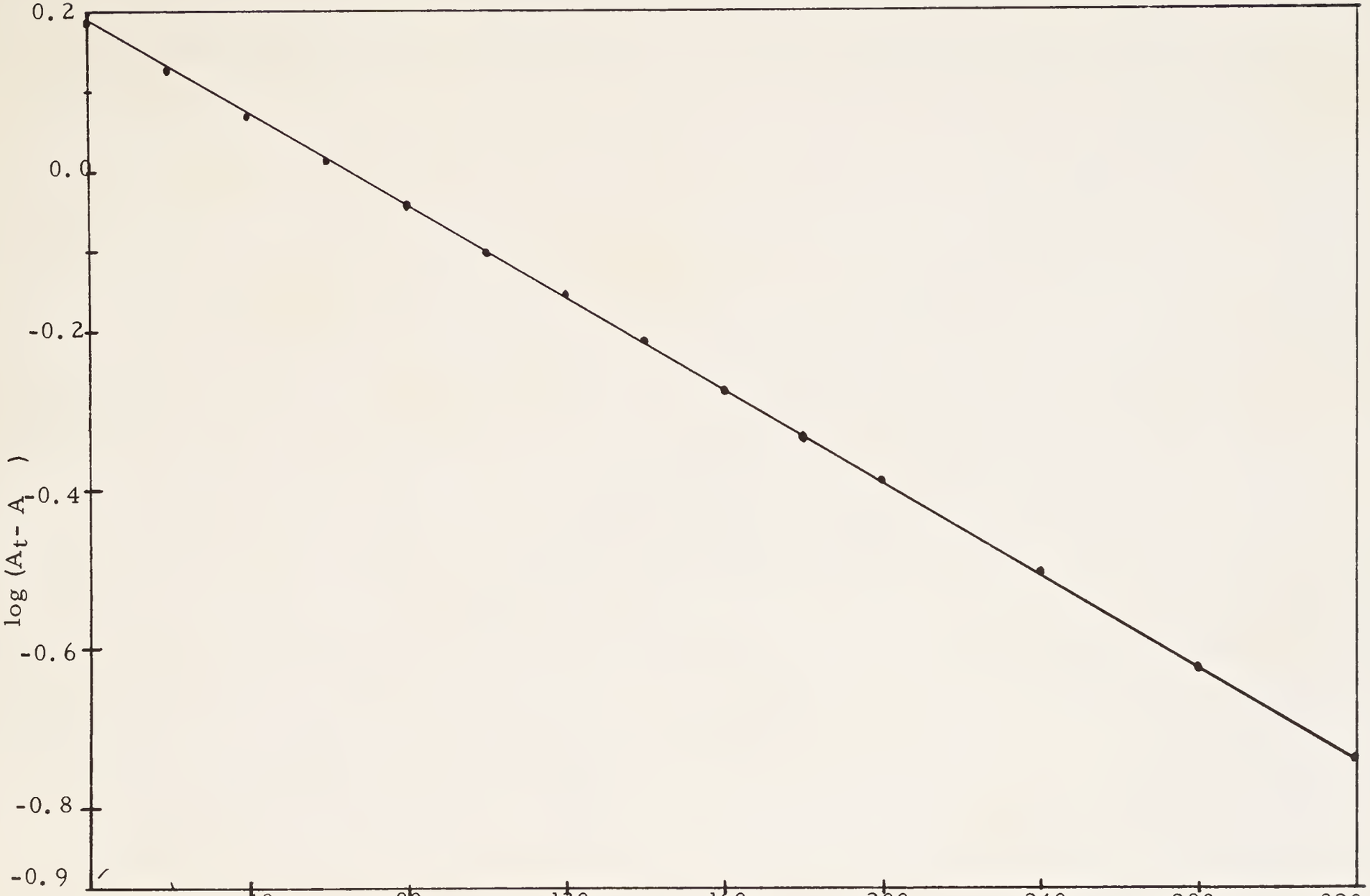


Fig. II-14.
Alkaline Hydrolysis of 1-benzyl-1-phenyl-2, 2, 3, 3-tetramethylphosphetanium bromide (100)
Concentration of NaOH 0.02 M. Pseudo first-order plot of log (A_t-A_∞) vs time. in water at 25°.

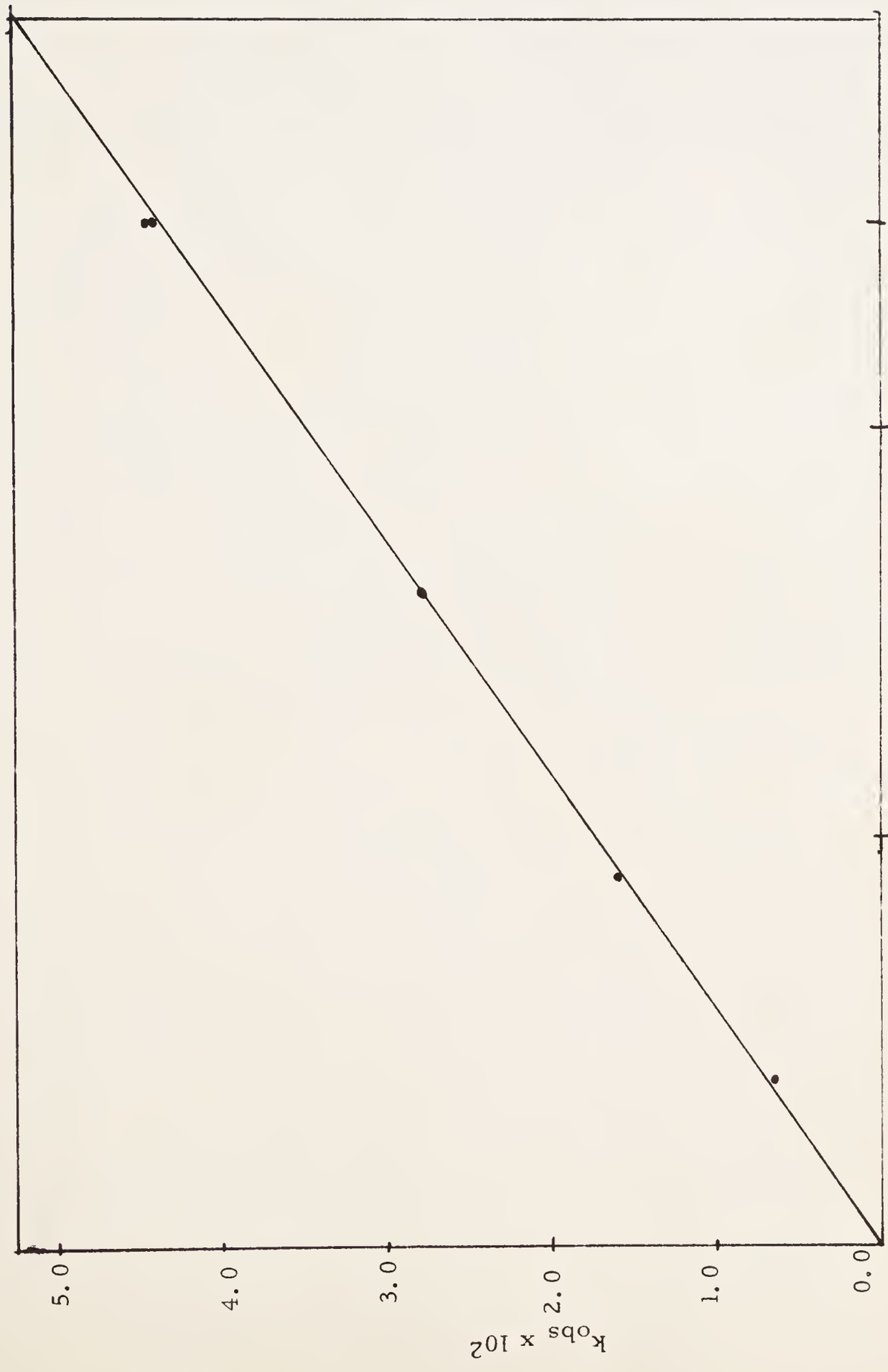


Fig. II-15.
Alkaline Hydrolysis of 1-benzyl-1-phenyl-2, 2, 3, 3-tetramethylphosphetanium bromide (100) at 25° in water. Plot of k_{obs} vs $[B]^2$

Table II-30. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in 50% ethanol-water at 24.9° by titrations, Ionic strength not constant. $A_o=B_o=0.005$ M.

Time Sec.	Conc. NaOH B. M.	$1/C^2-1/C_o^2$
165	2.98×10^{-3}	0.726×10^5
240	2.66	1.013
310	2.43	1.294
400	2.20	1.666
800	1.73	2.941
1200	1.46	4.291
1800	1.18	6.682
2400	1.10	7.800
3000	0.94	10.917

$k_3 = (1.798 \pm 0.055)x/0^2$ $M^{-2}Sec.^{-1}$

Table II=31. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in 50% ethanol-water at 24.9° by titration. Ionic strength not constant. A_oB_o=0.005 M.

Time Sec.	Conc. NaOH B M	$1/C^2 - 1/C_o^2$
75	3.70×10^{-3}	3.30×10^4
150	3.10	6.410×10^4
250	2.61	1.068×10^5
400	2.19	1.685×10^5
800	1.65	3.273×10^5
1200	1.40	4.702×10^5
1800	1.18	6.782×10^5
3000	0.92	10.680×10^5

$k_3 = 1.88 \pm 0.034 \times 10^2$ M.$^{-2}$ Sec.$^{-1}$

Table II-32. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in 50% ethanol-water at 5°. Ionic strength not constant. A_oB_o = 5.00×10^{-3}M.

Time Sec.	[B] Conc. NaOH M (Run #1)	$1/B^2 - 1/B_o^2$
300	4.110×10^{-3}	1.920×10^4
600	3.730×10^{-3}	3.880×10^4
900	3.460×10^{-3}	4.353×10^4
1200	3.210×10^{-3}	5.720×10^4
1800	2.900×10^{-3}	7.890×10^4
2400	2.580×10^{-3}	1.102×10^5
3600	2.300×10^{-3}	1.490×10^5
5500	1.990×10^{-3}	2.120×10^5
7000	1.770×10^{-3}	2.792×10^5

$k_3 = 1.89 \pm 0.0092 \times 10^1$ M.$^{-2}$Sec.$^{-1}$

Table II-33. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in 50% ethanal-water at 5°. Ionic strength not constant. $A_o = B_o = 5.00 \times 10^{-3}$M.

Time	[B] Conc. NaOH M (Run #2)	$1/B^2 - 1/B_o^2$
400	3.960×10^{-3}	2.380×10^4
1000	3.330×10^{-3}	5.020×10^4
2000	2.760×10^{-3}	9.130×10^4
3000	2.400×10^{-3}	1.336×10^5
4500	2.100×10^{-3}	1.868×10^5
6000	1.850×10^{-3}	2.522×10^5
9000	1.600×10^{-3}	3.506×10^5
15000	1.300×10^{-3}	5.517×10^5

$k_3 = 1.91 \pm 0.037 \times 10^1$ M.$^{-2}$Sec.$^{-1}$

Table II-34. Activation Parameters for Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide (94) in 50% ethanol-water.

Temperature °K	k_3M^{-2}Sec.$^{-1}$	$\Delta H^{\ddagger}$ kcal.deg^{-1}M^{-1}	$\Delta S^{\ddagger}$ e.u.
278.2	1.91×10^1		
278.2	1.88×10^1	18.3	+13.2
298.1	1.798×10^2		
298.1	1.88×10^2		

Table II-35. Alkaline Hydrolysis of 1-phenyl-1-2,2,3,3-pentamethyl-phosphetanium bromide (102) in 50% ethanol-water at 25°. $A_o=B_o=0.005$ M.

#	Time Sec.	Conc. NaOH B M.	$1/B^2$
1	1,800	4.4×10^{-3}	5.834×10^4
2	4,500	3.45	8.420×10^4
3	14,400	2.44	1.680×10^5
4	21,600	2.11	2.246×10^5
5	36,000	1.72	3.380×10^5

$k_3 = 4.075 \pm 0.059$ M.$^{-2}$ Sec.$^{-1}$

Table II-36. Alkaline Hydrolysis of 1-phenyl-1-2,2,3,3-pentamethyl-phosphetanium bromide (102) in 50% ethanol-water at 25°. $A_o=B_o=0.005$ M.

#	Time Sec.	Conc. NaOH B M	$1/C^2$
1	1,800	4.14×10^{-3}	5.834×10^4
2	4,500	3.49	8.210×10^4
3	14,400	2.45	1.666×10^5
4	21.600	2.10	2.268×10^5
5	36,000	1.73	3.341×10^5

$k_3 = 4.046 \pm 0.083$ M.$^{-2}$Sec.$^{-1}$

Table II-37. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution at 25.2°. Ionic strength 0.2M. $A_o=B_o=4.714 \times 10^{-3}$ M.

Time Sec.	[B] Conc. NaOH M (Run #1)	$1/B^2$
600	3.875×10^{-3}	6.66×10^{4}
1194	3.423×10^{-3}	8.535×10^{4}
2253	2.991×10^{-3}	1.118×10^{5}
3295	2.590×10^{-3}	1.491×10^{5}
4390	2.364×10^{-3}	1.789×10^{5}
5504	2.210×10^{-3}	2.047×10^{5}

$k_3 = 1.43 \pm 0.004 \times 10^{1}$ M.$^{-2}$Sec.$^{-1}$

Table II-38. Akkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetra methylphosphetanium bromide (100) in aqueous solution at 25.2°. Ionic strength 0.2M. $A_o=B_o=4.714 \times 10^{-3}$ M.

Time Sec.	[B] Conc. NaOH M (Run #2)	$1/B^2$
1104	3.516×10^{-3}	8.09×10^{-4}
2237	2.930×10^{-3}	1.165×10^{-5}
4276	2.354×10^{-3}	1.805×10^{-5}
5539	2.179×10^{-3}	2.106×10^{-5}
6760	1.943×10^{-3}	2.649×10^{-5}
7690	1.922×10^{-2}	2.707×10^{-5}

$k_3 = 1.50 \pm 0.07 \times 10^{1}$ M.$^{-2}$Sec.$^{-1}$

Table II-39. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution at 39.6°. Ionic strength 0.2M. $\overline{A_o=B_o}$ =4.714 x 10^{-3} M.

Time Sec.	[B] Conc. NaOH M (Run #1)	$1/B^2$
588	3.197×10^{-3}	9.784×10^{4}
1092	2.673×10^{-3}	1.399×10^{5}
1629	2.395×10^{-3}	1.743×10^{5}
2205	2.169×10^{-3}	2.126×10^{5}
2714	1.943×10^{-3}	2.649×10^{5}
3172	1.893×10^{-3}	2.794×10^{5}
3590	1.799×10^{-3}	3.090×10^{5}
4477	1.604×10^{-3}	3.887×10^{5}

$k_3 = 3.63 \pm 0.11 \times 10^{1}$ M.$^{-2}$Sec.$^{-1}$

Table II-40. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethyphosphetanium bromide (100) in aqueous solution at 39.6°. Ionic strength 0.2M. $A_o=B_o$ = 4.714 x 10^{-3} M.

Time Sec.	[B] Conc. NaOH M (Run #2)	$1/B^2$
595	3.21×10^{-3}	9.705×10^{4}
1200	2.615×10^{-3}	1.462×10^{5}
1800	2.275×10^{-3}	1.932×10^{5}
3605	1.770×10^{-3}	3.192×10^{5}
4207	1.688×10^{-3}	3.501×10^{5}
4841	1.627×10^{-3}	3.778×10^{5}

Table II-41. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution at 60°. Ionic strength 0.2M. $A_o = B_o = 4.714 \times 10^{-3}$ M.

Time Sec.	[B] Conc. NaOH M (Run #1)	$1/B^2$
80	3.480×10^{-3}	8.257×10^4
130	3.120×10^{-3}	1.027×10^5
175	2.820×10^{-3}	1.257×10^5
235	2.645×10^{-3}	1.429×10^5
357	2.285×10^{-3}	1.915×10^5
409	2.210×10^{-3}	2.047×10^5
468	2.090×10^{-3}	2.289×10^5

$k_3 = 1.85 \pm 0.045 \times 10^2$ M.^{2}Sec.$^{-1}$

Table II-42. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution at 60°. Ionic strength 0.2M. $A_o = B_o = 4.714 \times 10^{-3}$ M.

Time Sec.	[B] Conc. NaOH M (Run #2)	$1/B^2$
83	3.410×10^{-3}	8.600×10^4
161	2.915×10^{-3}	1.177×10^5
233	2.615×10^{-3}	1.462×10^5
299	2.417×10^{-3}	1.712×10^5
362	2.250×10^{-3}	1.975×10^5
429	2.115×10^{-3}	2.235×10^5
490	2.022×10^{-3}	2.446×10^5
600	1.857×10^{-3}	2.900×10^5

$k_3 = 1.96 \pm 0.012 \times 10^2$ M.$^{-2}$Sec.$^{-1}$

Table II-43. Activation Parameters for 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution. Ionic strength 0.2M.

Temperature ^{o}K	k_3 (Average) $M^{-2}Sec.^{-1}$	$\Delta H^{\ddagger}$ $kcal.deg^{-1}M^{-1}$	$\Delta S^{\ddagger}$ e.u.
298.2	1.47×10^{1}		
312.6	3.48×10^{1}	14.76	-5.55
333.0	1.89×10^{2}	$\pm$ 1.57	$\pm$ 0.67

Table II-44. Alkaline Hydrolysis of 1-benzyl-1,2,2,3,4,4-hexamethylphospetanium bromide (24) in 50% ethanol-water at 25%. Ionic strength 0.1M.

#	Conc. NaOH (OH^{-}), M.	$(OH^{-})^2$	k_{obs}, $Sec.^{-1}$
1	5.0×10^{-2}	2.5×10^{-3}	2.74×10^{-3}
2	6.25×10^{-2}	3.906×10^{-3}	4.03×10^{-3}
3	7.5×10^{-2}	5.625×10^{-3}	5.22×10^{-3}
4	8.25×10^{-2}	6.806×10^{-3}	8.09×10^{-3}
5	1.0×10^{-1}	1.0×10^{-2}	1.09×10^{-2}
6	1.0×10^{-1}	1.0×10^{-2}	1.109×10^{-2}

$k_3 = 1.09 \pm 0.03$ $M.^{-2}Sec.^{-1}$

Table II-45. Alkaline Hydrolysis of 1,1-dibenzyl-2,2,3,4,4-pentamethylphosphetanium bromide (26) in 50% ethanol-water at 25°. Ionic stren th 0.1M.

#	Conc. of NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	5.0×10^{-2}	2.5×10^{-3}	1.094×10^{-2}
2	5.0×10^{-2}	2.5×10^{-3}	1.041×10^{-4}
3	6.25×10^{-2}	3.096×10^{-3}	1.080×10^{-2}
4	7.5×10^{-2}	5.625×10^{-3}	2.637×10^{-2}
5	1.0×10^{-1}	1.0×10^{-2}	4.334×10^{-2}

$k_3 = 4.43 \pm 0.079$ M.$^{-2}$Sec.$^{-1}$

Table II-46. Alkaline Hydrolysis of 1-phenyl-1,2,2,3,4,4-hexamethylphosphetanium bromide (27) in 50% ethanol-water at 25°. Ionic strength 0.1M.

#	Conc. of NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	5.0×10^{-2}	2.5×10^{-3}	3.65×10^{-4}
2	5.0×10^{-2}	2.5×10^{-3}	3.53×10^{-4}
3	7.5×10^{-2}	5.625×10^{-3}	8.54×10^{-4}
4	7.5×10^{-2}	5.625×10^{-3}	8.62×10^{-4}
5	8.75×10^{-2}	7.656×10^{-3}	1.20×10^{-3}
6	1.0×10^{-1}	1.0×10^{-2}	1.54×10^{-3}

$k_3 = 1.54 \pm 0.013 \times 10^{-1}$ M.$^{-2}$Sec.$^{-1}$

Table II-47. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-phosphetanium bromide (94) in aqueous solution at 25%. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	5.0×10^{-2}	2.50×10^{-3}	1.54×10^{-4}
2	7.5×10^{-2}	5.625×10^{-3}	3.995×10^{-4}
3	7.5×10^{-2}	5.625×10^{-3}	3.995×10^{-4}
4	8.0×10^{-2}	6.40×10^{-4}	4.35×10^{-4}
5	9.0×10^{-2}	8.10×10^{-3}	5.30×10^{-4}
6	9.0×10^{-2}	8.10×10^{-3}	5.50×10^{-4}
7	8.5×10^{-2}	7.225×10^{-3}	4.83×10^{-4}

$k_3 = 6.80 \pm 0.10 \times 10^{-2}$ M.$^{-2}$Sec.$^{-1}$

Table II-48. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,4,4-pentamethylphosphetanium bromide in 50% ethanol-water at 25°. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	5.0×10^{-3}	2.5×10^{-5}	2.28×10^{-3}
2	5.0×10^{-3}	2.5×10^{-5}	2.12×10^{-3}
3	7.5×10^{-3}	5.625×10^{-5}	4.50×10^{-3}
4	1.0×10^{-2}	1.00×10^{-4}	8.20×10^{-3}
5	1.0×10^{-2}	1.00×10^{-4}	8.37×10^{-3}
6	1.5×10^{-2}	2.25×10^{-4}	1.79×10^{-2}

$k_3 = 8.13 \pm 0.032 \times 10^{+1}$ M.$^{-2}$Sec.$^{-1}$

Table II-49. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in aqueous solution at 25°. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, $Sec.^{-1}$
1	2.0×10^{-2}	4.0×10^{-4}	6.893×10^{-3}
2	2.0×10^{-2}	4.0×10^{-4}	6.725×10^{-3}
3	2.5×10^{-2}	6.25×10^{-4}	1.09×10^{-2}
4	3.0×10^{-2}	9.0×10^{-4}	1.603×10^{-2}
5	4.0×10^{-2}	1.6×10^{-3}	2.787×10^{-2}
6	5.0×10^{-2}	1.6×10^{-3}	4.422×10^{-2}
7	5.0×10^{-2}	2.5×10^{-3}	4.399×10^{-2}

$k_3 = 1.76 \pm 0.0055 \times 10^{1}$ $M.^{-2}Sec.^{-1}$

Table II-50. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3-tetramethylphosphetanium bromide (100) in 50% ethanol-water at 25°. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, $Sec.^{-1}$
1	1.0×10^{-3}	1.0×10^{-6}	2.31×10^{-3}
2	1.6×10^{-3}	2.56×10^{-6}	5.02×10^{-3}
3	1.6×10^{-3}	2.56×10^{-6}	5.14×10^{-3}
4	2.0×10^{-3}	4.0×10^{-6}	7.80×10^{-3}
5	3.0×10^{-3}	9.0×10^{-6}	1.87×10^{-2}
6	3.0×10^{-3}	9.0×10^{-6}	1.94×10^{-2}

$k_3 = 2.097 \pm 0.031 \times 10^{3}$ $M.^{-2}Sec.^{-1}$

Table II-51. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3,4-pentamethylphosphetanium bromide (101) in water at 25°. Ionic strength 0.1M.

#	Conc. of NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, $Sec.^{-1}$
1	6.0×10^{-2}	3.6×10^{-3}	2.73×10^{-3}
2	6.0×10^{-2}	3.6×10^{-3}	2.73×10^{-3}
3	7.0×10^{-2}	4.9×10^{-3}	3.68×10^{-3}
4	8.0×10^{-3}	6.4×10^{-3}	5.20×10^{-3}
5	8.0×10^{-3}	6.4×10^{-3}	5.00×10^{-3}
6	1.0×10^{-1}	1.0×10^{-2}	7.85×10^{-3}
7	1.0×10^{-1}	1.0×10^{-2}	7.42×10^{-3}

$k_3 = 7.70 \pm 0.092 \times 10^{-1}$ $M.^{-2}Sec.^{-1}$

Table II-52. Alkaline Hydrolysis of 1-benzyl-1-phenyl-2,2,3,3,4-pentamethylphosphetanium bromide (101) in 50% ethanol-water at 25°. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, $Sec.^{-1}$
1	4.0×10^{-3}	1.66×10^{-5}	2.09×10^{-3}
2	6.0×10^{-3}	3.60×10^{-5}	4.33×10^{-3}
3	8.0×10^{-3}	6.40×10^{-5}	9.03×10^{-3}
4	8.0×10^{-3}	6.40×10^{-5}	9.17×10^{-3}
5	1.0×10^{-2}	1.0×10^{-4}	1.43×10^{-2}
6	1.2×10^{-2}	1.44×10^{-4}	1.93×10^{-2}

$k_3 = 1.37 \pm 0.023 \times 10^{2}$ $M.^{-2}Sec.^{-1}$

Table II-53. Alkaline Hydrolysis of 1-phenyl-1,2,2,3,3-pentamethyl phosphetanium bromide (101) in 50% ethanol-water at 25°. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	2.0×10^{-2}	4.0×10^{-4}	1.09×10^{-3}
2	2.5×10^{-2}	6.25×10^{-4}	1.74×10^{-3}
3	2.5×10^{-2}	6.25×10^{-4}	1.77×10^{-3}
4	3.0×10^{-2}	9.0×10^{-4}	2.57×10^{-3}
5	3.0×10^{-2}	9.0×10^{-4}	2.50×10^{-3}
6	3.5×10^{-2}	1.225×10^{-3}	3.33×10^{-3}
7	4.0×10^{-2}	1.6×10^{-3}	4.52×10^{-3}

$k_3 = 2.82 \pm 0.026$ M.$^{-2}$Sec.$^{-1}$

Table II-54. Alkaline Hydrolysis of 1-benzyl-1-phenylphospholanium bromide (104) in 50% ethanol-water at 25%. Ionic strength 0.1M.

#	Conc. NaOH (OH^-), M.	$(OH^-)^2$	k_{obs}, Sec.$^{-1}$
1	5.0×10^{-2}	2.5×10^{-3}	2.886×10^{-4}
2	6.25×10^{-2}	3.906×10^{-3}	4.94×10^{-4}
3	7.5×10^{-2}	5.625×10^{-3}	6.89×10^{-4}
4	1.0×10^{-1}	1.0×10^{-2}	1.297×10^{-3}
5	1.0×10^{-1}	1.0×10^{-2}	1.313×10^{-3}

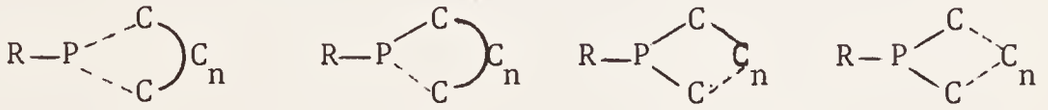
$k_3 = 1.29 \pm 0.0177 \times 10^{-1}$ M.$^{-2}$Sec.$^{-1}$

CHAPTER III

SYNTHESIS AND REACTIONS OF ∝-HALOMETHYLPHOSPHORUS COMPOUNDS

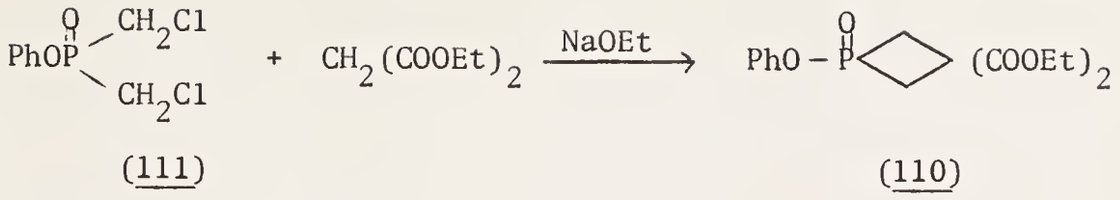
1. Introduction:

Three and four-membered phosphorus heterocycles have been synthesized by using several different routes. The various methods by which this can be accomplished have been reviewed [2]. In general, one can envision cyclization by the following general procedures in which the position of the ring closure is denoted by dotted lines:



I II III IV

Significant use of the first two approaches have been made [3]. In contrast, relatively little attention has been directed towards the methods illustrated in approaches III and IV. To date, procedure III has not been employed for the synthesis of the four-membered ring, although it has been used for the synthesis of larger rings [10]. There is only one example of procedure IV described in the literature; this was recently reported by a group of Russian workers [12]. In this example, a four-membered phosphorus heterocycle (110) has been generated by treating phenyl bis-(chloromethyl) phosphinate (111) with diethyl malonate in the presence of sodium ethoxide according to the scheme:

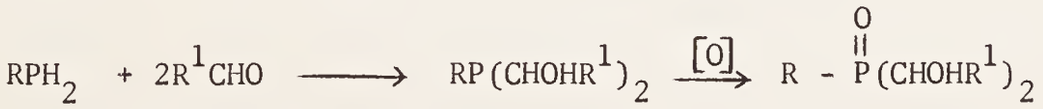


(111) (110)

It is apparent from the above discussion that the potential of procedure IV has not been fully realized. A likely starting material for such an approach would be a compound with an ∝-substituent adjacent to the phosphorus atom. In order to give a ring closure, the ∝-substituent should be moderately good leaving group. A possible example is illustrated in a compound with the general formula:

in which X and Z are replacable groups such as halogen and Y is oxygen, sulfur, a lone pair, etc.. A number of ∝-halomethylphosphorus compounds fall in this general category.

The synthesis of the ∝-halomethylphosphorus compounds poses a special problem. Many potential starting materials are derived from the condensation of carbonyl compounds with primary or secondary phosphines in the presence of an acid or a base [111]:



Recently, significant progress has been made in this direction [112,113]. One limitation of the reaction is that it involves at least three steps. Further, the condensation is reversible and thus certain reagents (e.g. PCl_5, $SOCl_2$) cannot conveniently be employed for the purpose of converting the

hydroxy compound to the halide derivative [9]. The procedure of Hellmann [114] which involves base decomposition of ∝-halomethylphosphonium salts to yield ∝-halomethylphosphine also suffers from limitations; low yields of the product are obtained in a mixture of compounds [114]:

$$PhP^{+}(CH_2Cl)_3\ Cl^- \xrightarrow{OH^-} Ph_2P(CH_2Cl)_2 + \underset{21\%}{}$$

$$PhP(O)(CH_2Cl)(CH_2CH_2CL) + CH_2O + HCl$$

51%

A similar result was found in this laboratory (p. 148):

$$(Ph)_2\overset{+}{P}(CH_3)-CH_2CL \xrightarrow{OH^-} Ph_2P\text{-}CH_3 + Ph_2P(O)CH_3$$

19%. 67%.

2. Results and Discussion:

The purpose of the present investigation was to synthesize compounds of the general formula:

$$(XCH_2)_n\ P(Y)(Z)_{3-n}$$

in order to circumvent some of the synthetic difficulties described above. The synthesis of a compounds with the general formula where n=1 was investigated an a working model. A model compound was deemed necessary in view of the unknown chemical behavior of ∝-halo substituents in these molecules. Initial studies were directed toward the introduction of substituents by the replacement of Z. Chloromethylphosphonyl dichloride (112) provided a convenient starting material for these studies. It may be mentioned here that although the end result of the synthesis of the small-membered ring by method 4 was not achieved during the course of this research, a number of useful substrates were prepared and several unprecedented reactions were inves-

tigated.

Nucleophilic substitutions at the phosphoryl center are quite well-known [115]. Treatment of (112) with phenyllithium resulted in the recovery of only polymeric material:

A more detailed examination of the compound (112) reveals that there is more than one possible site for attack. For example, the following reactions are conceivable:

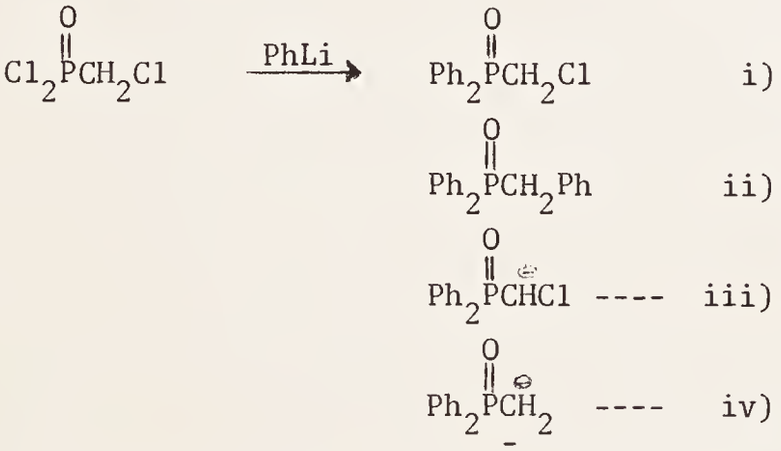
i) Nucleophilic substitution at phosphorus,

ii) Nucleophilic attack at carbon,

iii) Removal of the proton ∝-to phosphorus and subsequent reactions of the resulting carbanion,

iv) Halogen metal exchange and subsequent reactions of the carbarion.

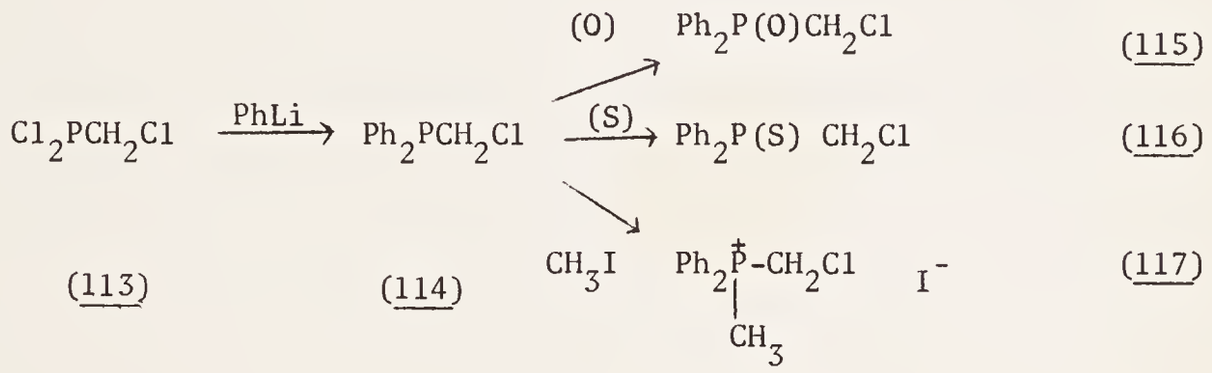
These reactions are illustrated below:



In order to avoid the side reactions, the phosphorus compound (113) in its lower oxidation state, e.g., the phosphine was selected (*). Chlorome-

(*) The acidity of the ∝-protons as well as the susceptibility of phosphorus nucleophilic attack is considerably reduced in phosphines compared to the phosphine oxide.

thylphosphonous dichloride (113) was successfully converted to diphenylchloromethylphosphine (114) in 60-65% yield by treatment with phenyllithium. Although the phosphine (114) could not be purified (due to its decomposition in the absence of solvent), it was readily converted to the corresponding phosphine oxide (115), phosphine sulfide (116) and the methiodide salt (117):



Similar results were obtained on treatment of (113) with phenylmagnesium bromide.

The evidence that the ∝-chloromethyl group in the phosphine (113) constitutes a potential site of attack by a nucleophile (see p138) came from the isolation of a small amount of the vinyl compound (118) formed from the reaction of (113) with an excess of phenyllithium followed by oxidation of the crude product with hydrogen peroxide. Treatment of chloromethyldiphenylphosphine (114) with phenyllithium followed by oxidation also gave the same compound in low yields. The formation of compound (118) may be rationalized by the following mechanism:

$$Ph_2P\text{-}CH_2Cl \xrightarrow{PhLi} Ph_2P\text{-}\overset{-}{C}HCl \xrightarrow{Ph_2PCH_2Cl} Ph_2P\text{-}CH_2\text{-}CHClP\text{-}Ph_2$$

$$\downarrow \text{PhLi}, \downarrow -\overset{+}{H}, Cl^-$$

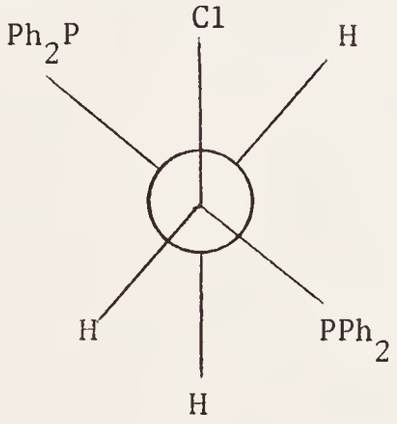
$$Ph_2P\text{-}CH{=}CH\text{-}PPh_2$$

$$\downarrow (O)$$

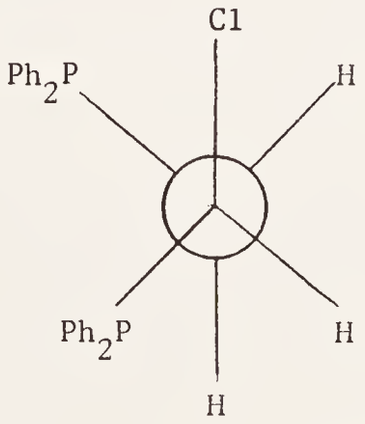
$$Ph_2P(O)\text{-}CH{=}CH\text{-}P(O)Ph_2$$

(118)

Examination of the conformations of the intermediate phosphine reveals that a predominant formation of the trans isomer should occur, as was found. This is because the intermediate (119) trans isomer would involve less steric interaction of the bulky substituents than (120) which would lead to the cis isomer:



(119)



(120)

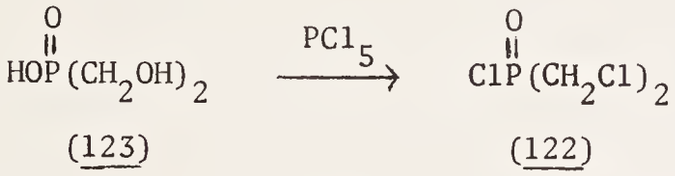
A carbene mechanism could also rationalize the results.

During the synthesis of ∝-chloromethyl phosphorus compounds, a one step method for the preparation of bis-(chloromethyl) phenylphosphine oxide (121) was achieved in 50% yield using phenylmagnesium bromide:

$$ClP(O)(CH_2Cl)_2 \xrightarrow{PhMgBr} PhP(O)(CH_2Cl)_2$$

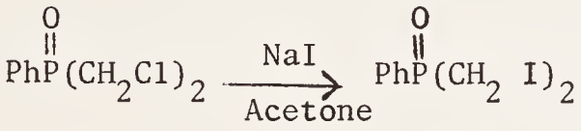
(122) (121)

The requisite phosphinyl chloride (122) was conveniently prepared in 56% yield by the chlorination of the commercially available bis-(hydroxymethyl) phosphinic acid (123) with phosphorus pentachloride:



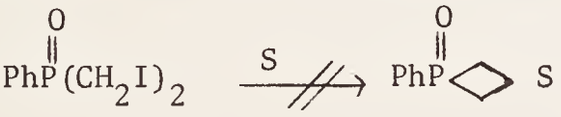
(123) (122)

In view of the requirement of a good leaving group, bis-(iodomethyl) phenylphosphine oxide (124) was prepared. The iodination was achieved under milder conditions than described by Yagupolski [116]. These workers treated (121) with sodium iodide in refluxing ethylene glycol for 6 hr.:



(121) (124)

The possibility of nucleophilic substitution at the α-carbon site in these compounds, as shown above, was the basis of the attempted reaction of compound (121) with azide, thiophenoxy and of (124) with cyanide ions. The starting material was recovered in each case. An attempt to prepare a four-membered ring containing both sulfur and phosphorus, patterned after a procedure by Newmann [117], did not yield any cyclic product:



Attempted cyclization with disodium EDTA [118] as well as $FeCl_3/C_2H_5MgBr$ [119] also failed to yield any cyclic product; only the reduction dimethylphenylphosphine oxide (125) was isolated:

$$PhP(O)(CH_2Cl)_2 \xrightarrow[C_2H_5MgBr]{FeCl_3} PhP(O)(CH_3)_2 + \text{No } PhP(O)\triangleleft$$

(125)

$$PhP(O)(CH_2I) \xrightarrow[\text{etc}]{Na_2EDTA} PhP(O)(CH_3)_2 + \text{No } PhP(O)\triangleleft$$

(125)

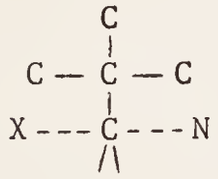
Some of the above results are quite surprising in view of the know nucleophilic substitution in similar compounds [120]. However, Hojo and Yoshida [121] have studied the reactivity of ∝-chloromethyl sulfoxide (126) and sulfone (127). The rate of displacement of chloride by iodide in these compounds was compared to that of n-butyl chloride. It was observed that although ∝-chloroacetophenone reacted 10^5 times faster than n-butyl chloride, ∝-chloromethyl sulfoxide (126) and sulfone (127) reacted one-hundred times slower than n-butyl chloride.

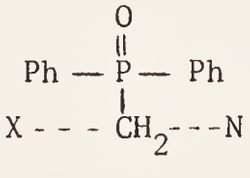
The ∝-chloromethyldiphenylphosphine oxide (115) has also been found to exhibit a similar lack of reactivity towards nucleophilic displacement of chloride by iodide. The oxide (115) was found to react 30-40 times slower than n-butyl chloride (Table 1). The difference in the reactivity of ∝-chloromethyl carbonyl, sulfonyl, sulfinyl and phosphoryl compounds cannot be rationalized on the electronic effects since the latter are very similar in these compounds [121]. The large difference between ∝-chlorocarbonyl compounds and the other heterocompounds can be rationalized on the basis of a steric effect, commonly known as a "neo-pentyl effect" [87]. Thus, all the substituent groups (e.g., carbonyl, phosphoryl, sulfinyl and sulfonyl), due to their electron withdrawing nature, facilitate the attack of the nucleophile at the ∝-carbon atom. However, the carbonyl compound with sp^2 geometry

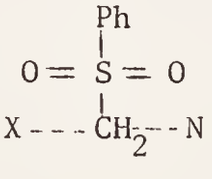
provides less steric hindrance to the attacking reagent than sulfones and phosphineo/oxides, since they have tetrahedral geometry. As a result of this geometry, the latter are very similar to neo-pentyl chloride. This leads to steric blocking of the attacking reagent as illustrated below:

Table III-1. Relative Rates of Nucleophilic Substitution in Chloromethyl Derivatives.

Compound	Relative Rate 50°	80°
n-Butyl Chloride	1	1
$Ph\text{-}CO\text{-}CH_2Cl$	$<1.05 \times 10^5$	
$Ph\text{-}SO\text{-}CH_2Cl$	<0.01	
$Ph\text{-}SO_2\text{-}CH_2Cl$	<0.02	
$Ph_2\text{-}PO\text{-}CH_2Cl$		<0.03







This, however, is not the complete explanation since, the lack of reactivity of the sulfoxides cannot be rationalized on the same grounds [121].

In the course of this investigation, an interesting reaction was observed during an attempt to oxidize the chloromethylphosphine (114) to the corresponding oxide (115). The reaction was thought to be sufficiently unusual as to merit a more detailed study. Thus, treatment of (114) with hydrogen peroxide in acetone yielded the chloromethylphosphine oxide (115):

$$Ph_2PCH_2Cl \xrightarrow[\text{Acetone}]{H_2O_2} Ph_2P(O)CH_2Cl$$

(114) (115)

On the other hand, oxidation in glacial acetic acid, followed by evaporation of the solvent, treatment with water and extraction of the product with benzene afforded diphenylmethylphosphine oxide (128):

$$Ph_2PCH_2Cl \xrightarrow[H_2O_2]{CH_3COOH} Ph_2\overset{O}{\overset{\|}{P}}-CH_3$$

(114) (128)

On further examination, it was found that hydrogen peroxide was not involved as a reactant since the same product (128) was obtained by heating (114) with glacial acetic acid at 80° followed by the previous work-up procedure. The replacement of the chlorine atom by hydrogen was suggestive of some type of a hydride transfer mechanism. Based on this mechanistic assumption, the phosphine (114) was treated with acetic acid-d_4 followed by work-up H_2O to obtain a nearly quantitative incorporation of one atom of deuterium in the oxide (128). A control experiment (see Table 2) with acetic acid/D_2O and acetic acid/H_2O showed that the deuterium atom transferred during the process was the one from the acetic acid-d_4:

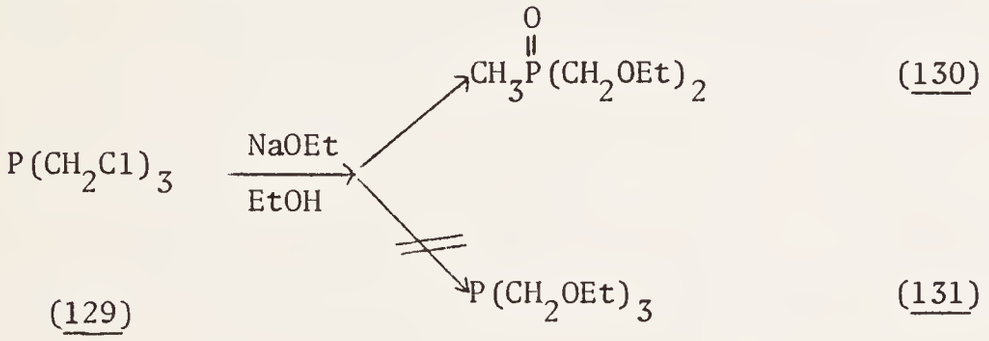
$$Ph_2PCH_2Cl + D_3CCOOD \xrightarrow{\Delta} Ph_2\overset{O}{\overset{\|}{P}}-CH_2-D$$

(*) The purpose of the oxidation was to obtain the corresponding oxide which was to be used in the model study.

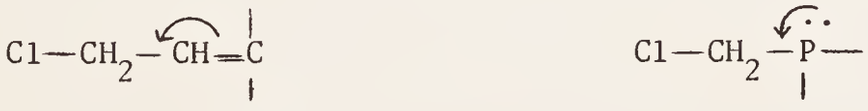
The course of deuterium incorporation was conveniently followed by nmr integration.

Related to this observation is the important work of Kabachnik, Griffin and Goldwhite. Most of their research involved a similar displacement of chloride, but under basic reaction conditions. It would be pertinent to review some of these studies related to results here.

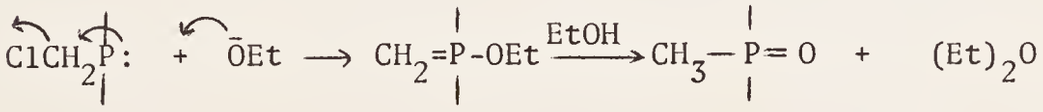
Kabachnik and co-workers [122] treated tris-(chloromethyl) phosphine (129) with sodium ethoxide and obtained bis-(ethoxymethyl)methylphosphine oxide (130) instead of the expected tris-(ethoxymethyl)phosphine (131):



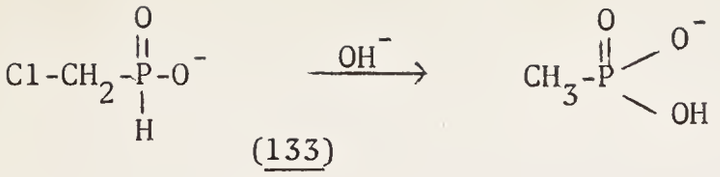
Kabachnik [122] proposed that a "pseudoallylic" rearrangement was responsible for the reaction, since there is an analogy between the following two electronic structures:



The pseudoallylic rearrangement may be visualized to occur as follows:



Griffin and co-workers [123] showed that in thh presence of base, chloromethylphosphinic acid (133) rearranged to methylphosphonic acid (134):

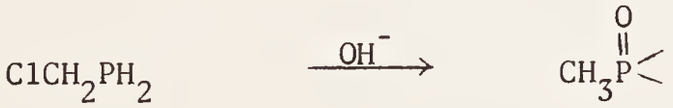


(133)

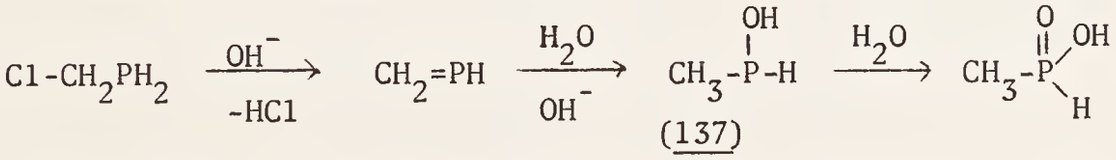
However, contrary to the pseudoallylic rearrangement proposed by Kabachnik [122], Griffin showed by isotopic labelling, that the predominant reaction took the following course [124]:

Thus, most of the deuterium in the starting phosphinic acid (133) was found in the methyl group of the product, conclusively demonstrating that the hydride transfer occurred through an intramolecular process.

A similar base-induced rearrangement of chloromethylphosphine (135) to methylphosphinic acid (136) has been reported by Goldwhite and co-workers [125]:

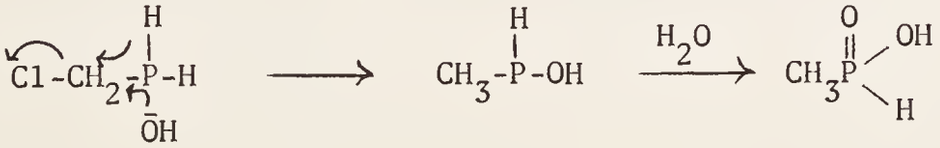


On the basis of the analogy to reactions of polyfluorophosphonous dichloride, Goldwhite proposed a phosphaalkene (137) as an intermediate:



(137)

This analogy may not be exactly parallel since nucleophilic attack on trivalent phosphines is known to occur and because the hydride migration shown below, would essentially give the same results:



However, no isotopic labelling experiments were performed to determine whether the mechanism involved an intramolecular hydride transfer or a phosphaalkene intermediate.

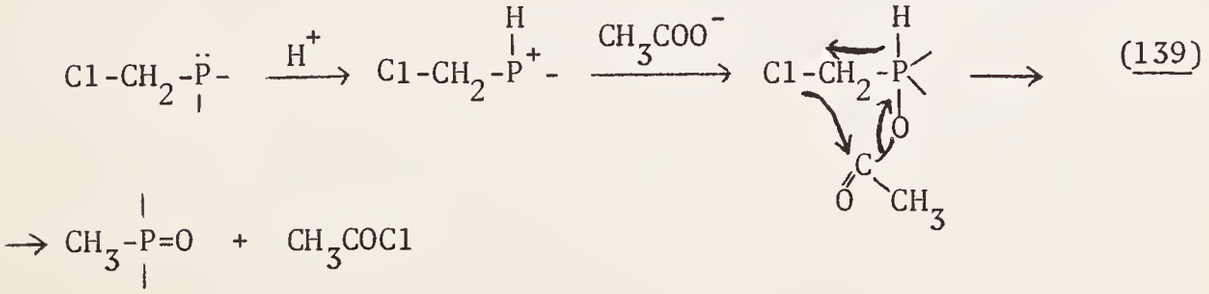
During the rearrangement of (114), some experimental difficulty was encountered because of its instability, especially in the absence of solvent. A more satisfactory compound was selected for carrying out quantitative work, namely tris-(chloromethyl)phosphine (129) which could be distilled under vacuum with slight decomposition. Similar to (114), the phosphine (129) also led to incorporation of approximately one atom of deuterium in the oxide product (138) on treatment with acetic acid-d_4:

$$(ClCH_2)_3P + D_3CCOOD \longrightarrow D\text{-}CH_2\text{-}P(=O)(CH_2Cl)_2 \qquad (138)$$

Approximately equivalent amounts of phosphine (129) and glacial acetic acid were sealed in an nmr tube under vacuum and heated for 27 hr. at 131°. The products were found to be acetyl chloride (91.6 mole %), acetic anhydride (8.4 mole %) and bis-(chloromethyl)methylphosphine oxide (138):

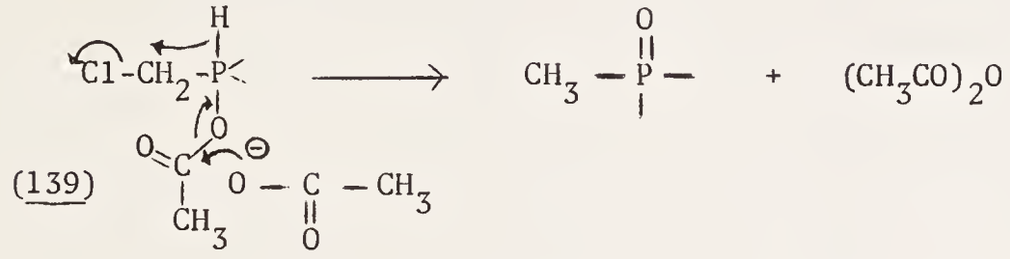
$$P(CH_2Cl)_3 + CH_3COOH \xrightarrow{\Delta} \underset{91.6\%}{CH_3COOCl} + \underset{8.4\%}{(CH_3CO)_2O} + \underset{(138)}{CH_3P(=O)(CH_2Cl)_2}$$

This led to the following mechanism:

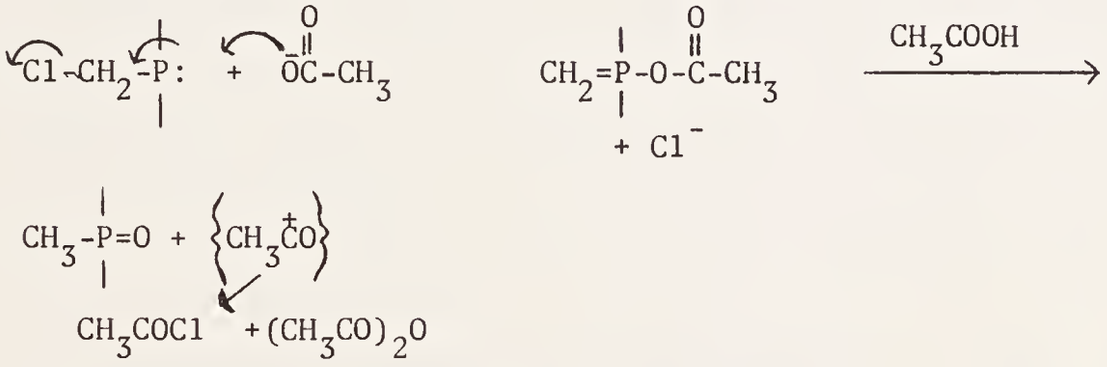


(139)

The production of the small amount of acetic anhydride may be rationalized by the attack of acetic acid or its anion on the pentacovalent intermediate (139):



The above evidence, of course, does not rule out the possibility of a pseudoallylic mechanism illustrated below:



However, one would predict that the formation of acetic anhydride in the pseudoallylic mechanism, would be significant because in the early stages of the reaction, the concentration of chloride ions would be much less than that of acetic acid. In any event, definite proof for determining which mechanism operates may possibly be obtained by carrying out the experiment in the presence of external $^{37}Cl^-$ ions. The pseudoallylic mechanism should lead to almost 50% incorporation of ^{37}Cl in the acetyl chloride, whereas the proposed mechanism requires no incorporation of ^{37}Cl since the formation of acetyl chloride is intramolecular. This assumes lack of exchange of chloride ion with acetyl chloride.

3. Experimental.

Synthesis of Chloromethyldiphenylphosphine(114). To a stirred solution of 15.2g (0.1 mole) of chloromethylphosphonous dichloride (113) in 200 ml petroleum ether (30-60°) was added 90 ml of 2.58M phenyllithium (2.2 equivalent) in 3:1 benzene ether over 115 min. at -65° under a nitrogen atmosphere. A pale yellow precipitate slowly accumulated as the addition progressed. The mixture was stirred for an additional 40 min. and then warmed to -10-0° by removing the cold bath. The reaction was quenched with 100 ml of ice water while stirring and the mixture was allowed to stir for an additional 3 hr.. The two layers were separated, the aqueous layer was extracted with ether and the combined organic layers were washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent (see p.132) gave 31.6g mobile liquid which contained some solvent. The nmr of the crude liquid (benzene) showed peaks at: τ=1.83-2.50 (10H, m, aromatic), τ=5.95 (2H, d, $^{2}J_{PCH}$=6.0 cps).

Preparation of Chloromethyldiphenylphosphine Oxide (115). The crude liquid obtained above was dissolved in 60 ml acetone and oxidized by adding 16 ml of hydrogen peroxide (30%) with stirring at 10°. The acetone was evaporated and the residue was dissolved in 30 ml benzene. The two layers were separated and the organic layer was dried over anhydrous sodium sulfate. Evaporation of benzene gave 22.8g of a viscous liquid wiich solidified on scratching. Recrystallization from methanol-water followed by sublimation at 120° (0.2 mm) gave 20g of a crystalline solid m.p. 130° forms murky liquid which clears at 136-137° (136-137°)(114)(50%). The nmr ($DCCl_3$) showed peaks at: τ=1.90-2.80 (10H, m, aromatic), τ=5.95 (2H, d, $^{2}J_{PCH}$=6.3 cps).

Treatment of (114) with Sulfur. To the crude phosphine prepared from 15.2g (0.1 mole) of (113) and 90 ml phenyllithium as outlined on p. 142 , was added 6.4g (0.2g atom) sulfur and 160 ml of benzene and the resulting mixture was allowed to reflux for 3 hr. under a nitrogen atmosphere. The mixture was cooled, filtered, and the solvent was evaporated to obtain 25.6g of semi-solid. The product was extracted with hot cyclohexane and recrystallized by concentration of the solvent to give 5.6g of yellow crystals, m.p., 76-78° (21.6%. The nmr ($DCCl_3$) showed peaks at τ=1.90-280 (10H, m, aromatic), τ=5.85 (2H, d $^2J_{PCH}$=6.0 cps). Anal. Calcd. for $C_{13}H_{12}ClPS$: C, 58.55; H, 4.54; P, 11.62. Found: 58.34; H, 4.47; P, 11.82.

Quaternization of Phosphine (114) with Methyl Iodide. To a solution of the crude phosphine (114)(obtained from 22.7g (113) and phenyllithium) in 250 ml anhydrous ether, was added 6-10 fold excess of methyl iodide and the mixture was stored in the dark for 48 hr.. The precipitate was filtered, washed with ether and then recrystallized from methanol-ether (using Norit) to obtain 48.4g crystalline solid (117) m.p. 203-205° (with decomposition) Yield 67.5%. The nmr (CF_3COOH) showed peaks at: τ=1.20-1.86 (10H, m, aromatic), τ=4.74 (2H, d, $^2J_{PCH}$=7.0 cps), τ=7.06 (3H, d, $^2J_{PCH}$=15.0 cps). Anal. Calcd. for $C_{14}H_{15}Cl$: C, 44.65; H, 4.01; I, 33.69; P, 8.22. Found: C, 44.80; H, 4.11; I, 33.72; P, 8.39.

Reaction of (113) with Phenylmagnesium Bromide. A solution of phenylmagnesium bromide was prepared from 23.5g (0.16 mole) of bromobenzene and 4.0g (0.165g atom) of magnesium turnings in 150 ml of ether.

To a stirred solution of 3.8g of chloromethylphosphonous dichloride (113) in 100 ml of petroleum ether (30-60°) at -65° was added the above Grignard reagent over 2 hr. under an atmosphere of nitrogen. The mixture

was stirred for an additional 10 min. and quenched with 50 ml of distilled water. Gradual warming of the mixture to room temperature gave a thick emulsion which was cleared by adding a saturated solution of ammonium chloride and an excess of ether. The two layers were separated, the aqueous layer extracted with ether, and the combined organic layers were washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a semi-viscous liquid which was dissolved in ether and treated with an excess of methyliodide. The mixture was stored in the dark for 48 hr.. The precipitate was filtered, washed with ether and recrystallized from methanol-ether to give 6.3g (67%) of crystalline solid (117) m.p. 203-206°. A mixture m.p. with the authentic compound did not show any depression. The nmr was identical to that of an authentic compound (117).

Preparation of Bis-(Chloromethyl)phosphinyl Chloride (122). To a vigorously stirred suspension of 625g (3.0 mole) of phosphorus pentachloride in 1500 ml of chloroform in a three-necked flask was added at 15°C 126g (1.0 mole) of bis-(hydroxymethyl)phosphinic acid (123) over 35 hr.. The acid in the addition funnel was occassionally warmed to prevent crystallization. The resulting clear solution was stirred for an additional 7 hr.. Evaporation under vacuum followed by distillation of the liquid gave 102.4g (56.0%) of a colorless liquid b.p. 75-80 (0.3-0.4 mm) (98-101/1 mm) (126). The nmr (CCl_4) showed peaks at: τ=5.83 (d, $^2J_{PCH}$=6.5 cps).

Treatment of (122) with Phenylmagnesium Bromide, Preparation of Bis-(Chloromethyl)phenylphosphine Oxide (121). Phenylmagnesium bromide was prepared from 47.1g (0.3 mole) of bromobenzene and 7.2g (0.3g atom) of magnesium turnings in 175 ml anhydrous ether.

The above Grignard reagent was added to a solution of 36.3g (0.2 mole) of bis-(chloromethyl)phosphinyl chloride (122) in 200 ml of ether at -65°

with stirring under an atmosphere of nitrogen over 75 min.. A white precipitate formed which made the mixture difficult to stir. A 100 ml portion of ether was added and the mixture was allowed to stir for an additional 1 hr.. The reaction was quenched with 150 ml of water and then the mixture was allowed to warm up to room temperature with stirring (to break the lumps of the solid).

Filtration and recrystallization from methanol (using Norit) gave 22.8g (50%) of needles, m.p. 142-143° (141-142°)(116). The nmr ($DCCl_3$) showed peaks at: τ=1.80-2.60 (5H, m, aromatic), τ=6.00 (4H, d, $^2J_{PCH}$= 7.0 cps).

Preparation of Bis-(Iodomethyl)phenylphosphine Oxide (124). To a hot solution of 1.1g (0.005 mole) of the oxide (121) in 25 ml of acetone was added 5.8g (0.04 mole) of sodium iodide in one portion and the mixture was allowed to reflux for 24 hr.. A white precipitate appeared. After cooling, the mixture was poured over 100g of ice. The precipitate was filtered, washed with cold water, and dried in air to give 1.5g (75%) of a pale yellow crystalline solid, m.p. 169-170°. Recrystallization from benzene-petroleum ether (30-60°) raised the m.p. 171-173° (172-173°) (116). The nmr (CF_3COOH) showed peaks at: τ=2.10-2.90 (5H, m, aromatic), τ=6.54 (4H, d, $^2J_{PCH}$=6.5 cps).

Attempted Reaction of (121) with Sodium Azide. A mixture of 1.12g (0.005 mole) of oxide (121), 1.0g of sodium azide and 10 ml of DMF was heated to reflux for 24 hr.. After cooling, the mixture was poured over 100g of ice. The precipitate was filtered to give 1.0g of the starting material. (Recovery 89%).

Attempted Reaction of (124) with Sodium Cyanide. A solution of 4.06g (0.01 mole) of (124) in hot methanol was added to a solution of 1.0g (0.02 mole) of sodium cyanide in 6 ml of water and the mixture was heated to reflux for 12 hr., cooled and filtered to obtain dark brown filtrate. Evaporation of the solvent gave a dark brown semi-dolid. The residue was extracted with chloroform, and the combined organic layers dried over anhydrous sodium sulfate and evaporated to yield 2.4g (60%) starting material, characterized by its ir and nmr.

Attempted Reaction of (124) with Sodium Sulfide. A sample of sodium sulfide was recrystallized and dried by the procedure of Newman [117].

To 2.1g (0.052 mole) 0f (124)in 30 ml of ethyl cellosolve was added to a solution of 1.25g of anhydrous sodium sulfide in 18 ml ethylene glycol over 14 min.. The mixture was allowed to stir for 70 hr. and the solvent was removed under vacuum (90° at 0.05 mm). The residue was dissolved in chloroform, the organic layer was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a polymeric material that could not be characterized.

Attempted Reaction of (121) with Sodium Thiophenolate. A solution of sodium thiophenolate was prepared by treating 2.2g (0.02 mole) of thiophenol with a solution of 0.46 (0.02g atom) of sodium in 40 ml of ethanol followed by refluxing the mixture for one half hr.

To the above solution was added 1.12g (0.005 mole) of the oxide (121) in portions. The mixture was refluxed for 3 hr; a precipitate formed during this period. The solvent was evaporated and the residue extracted with carbon disulfide and evaporated, to produce a resinous mass which could not be characterized.

Attempted Cyclization (121) with $FeCl_3/C_2H_5MgBr$. A solution of ethylmagnesium bromide was prepared from 32.5 g (0.3 mole) of ethyl bromide and 7.5g (0.315g atom) of magnesium turnings in 200 ml ether.

To a stirred solution of 11.2g (0.05 mole) of bis-(chloromethyl)phenylphosphine oxide (121) in 100 ml of ether in a four-necked round bottomed flask equipped with a water condenser, were added simultaneously, the above Grignard reagent and a solution of 0.7g of anhydrous ferric chloride in 50 ml of ether over 75 min. A dark brown metal deposited on the side of the flask. The exothermic reaction was stirred overnight and then quenched by adding a slurry of 200 ml of 2M HCl saturated with ammonium chloride and ice, until two clear layers were obtained. The ether layer was separated, washed with water dried and evaporated; no residue was obtained. The aqueous layer was extracted with methylene chloride and the combined organic layers were dried over anhydrous sodium sulfate and evaporated to give 7.0g (91%) of pale brown solid. Recrystallization from cyclhexane gave 6.0g crystalline solid m.p. 102-103 clearing at 105-107° (110°) [128]. The nmr ($DCCl_3$) showed peaks at: τ=1.90-2.70 (5H, m, aromatic), τ=8.30 (6H, d, $^2J_{PCH}$=13.0 cps). The compound was identical to dimethylphenylphosphine oxide (125).

Attempted Cyclization of Bis-(Iodomethyl)phenylphosphine Oxide (124). A mixture of 4.04g (0.01 mole) of (124), 1.3g (0.0435 mole) of disodium EDTA, 3.45g (0.086 mole) sodium hydroxide, in 6 ml of water, 0.28g of sodium iodide, 2.56g (0.039g atom) of zinc powder and 20 ml of 95% ethanol was heated to reflux for 1 hr. in an oil bath at 120°. The mixture was cooled, 150 ml of 95% ethanol added. The reaction was then heated to reflux and the mixture was filtered hot. The solvent was evaporated, water was added to the residue followed by extraction with chloroform.

The chloroform layer was dried over sodium sulfate, and evaporated to give 2.2g of liquid that solidified on cooling. Recrystallization from cyclohexane gave 1.4g (94%) of white needles, m.p. 100-102 (murky liquid clearing at 105-107°) (100°) [128]. The nmr of the compound was identical to that of an authentic sample of (125).

Preparation of trans-1,2-Vinylenebis(diphenylphosphine) Dioxide (118). The crude phosphine (114) was prepared from 7.6g (0.05 mole) of (113) and 50 ml of 2.58 M phenyllithium as described earlier and aas evaporated to 16.6g of liquid. The above liquid was dissolved in 25 ml of ether and treated with 25 ml of 2.58 M phenyllithium (3:1, benzene:ether) at -30° over 50 min.. The mxiture was allowed to warm up to 15° and quenched with 25 ml of water. The two layers were separated, the aqueous layer was extracted with benzene and the combined organic layers were dried over anhydrous sodium sulfate. Evaporation of the solvent gave 13.0g of the crude phosphine which was dissolved in 25 ml of acetone and oxidized with 30% hydrogen peroxide solution until a positive starch-iodide test was obtained. The solvent was evaporated and the residue was treated with 100 ml of benzene when an insoluble solid precipitated. Filtration gave 1.1g (5.1%) of product. Recrystallization from 95% ethanol gave 0.62g of a crystalline solid m.p. mmp. 306-309° (306-309°) [127]. The nmr (CF_3COOH) identical to that of an authentic compound (Provided by A. Aquiar of Tulane Univ. [127]).

The benzene layer was dried and evaporated to give 11.1g of (115) characterized by mmp. with an authentic sample.

Alkaline Decomposition of Chloromethylmethyldiphenylphosphonium Iodide (117). A mixture of 4.0g (0.01 mole) of powdered (117), 20 ml of water, 30 ml of benzene and 5 ml of methyl iodide was stirred under an atmosphere of

nitrogen. To this mixture was added 15 ml of 5% sodium hydroxide solution and the stirring was continued for 48 hr.. A precipitate was formed which was filtered and washed with a small amount of benzene to yield 0.65g (19.0%) of a solid which was recrystallized from acetonitrile-ethyl acetate to give a crystalline solid, m.p. 248.5-249.5° (241°) [129] (mmp). The nmr (F_3CCOOH) showed peaks at: τ=1.90-2.46 (10H, m, aromatic), τ=7.40 (6H, d, $^2J_{PCH}$= 14.0 cps). The sample was identical to an authentic sample of dimethyldiphenylphosphonium iodide [129].

The layers in the filtrate were separated, the layer was extracted with benzene and the combined benzene layers were washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent and recrystallation of the residue from cyclohexane gave 1.55g (67.5%) of white needles, m.p. 109-110.5° (109-111°) [130]. The nmr ($DCCl_3$) showed peaks at: τ=2.00-2.75 (10H, m, aromatic), τ=8.00 (3H, d, $^2J_{PCH}$=13.3 cps.). The compound was characterized as diphenylmethylphosphine oxide (128) by mmp.

Preparation of Diphenylmethylphosphine Oxide (128), Reaction of (114) with Acetic Acid. To the crude phosphine (114) containing benzene, prepared from 15.2g of (113) and phenyllithium as shown earlier (p.142) was added 15 ml of glacial acetic acid and the mixture was heated under an atmosphere of nitrogen for 3 hr. at 60-80°. The solvent was evaporated in vacuo. The thick oily residue was treated with water and extracted with benzene several times; the combined benzene layers were washed with water and dried over anhydrous sodium sulfate. Evaporation gave 9.8g of a viscous liquid. The liquid was extracted with hot cyclohexane (Norit) and concentrated to give white needles m.p. 110-110°(109-111°) [130]. The yield of the pure diphenylmethylphosphine oxide (128) was 3.4g (47.7%). The nmr ($DCCl_3$) was identica

to that of an authentic sample.

Control Experiments on Deuterium Exchange. Approximately 2.0g of an aliquot of the phosphine (114)(prepared as on p.142) was treated with an equivalent amount of acetic acid-d_4 and the mixture was heated at 60-80° for 3 hr.. The volatile material (solvent, acetyl chloride, ect.) was evaporated and the residue was treated with a slight excess of D_2O and then allowed to stand for 10 min. The resulting suspension was processed as on p. 149.

In an analogous manner, a 2.0g aloquit was treated with acetic acid and then quenched with D_2O. The resulting mixture was processed as on p.149 . The results of the deuterium exchange reactions are summarized in table III-2.

Tris-(chloromethyl)phosphine (129) was prepared by the method of Hoffman [124] by an alkaline decomposition of tetrakis-(chloromethyl) phosphonium chloride. The latter was synthesized as follows. To a suspension of 150g (0.72 mole) of phosphorus pentachloride in 400 ml carbon tetrac loride was added 27.5g (0.14 mole) of tetrakis-(hydroxymethyl)phosphonium chloride through a wide-mouth addition funnel with stirring over 5 min.. The mixtu e was allowed to reflux for 7 hr.. On cooling, a crystalline solid precipitated. The mixture was diluted with an equal volume of ethyl acetate, and filtered and recrystallized from methanol-ethyl acetate to give 28.5g (75%) of a crystalline solid, m.p. 202-203° (192-193°) [131]. The nmr (CF_3COOH) showed peaks at: τ=5.26 (8H, d, $^2J_{PCH}$= 5.7 cps).

Treatment of tris-(Chloromethyl)phosphine (129) with Acetic Acid, Preparation of (138). To 3.06g (0.05 mole) of glacial acetic acid in a round bottomed flask was added 4.5g (0.025 mole) of the phosphine (129),

Table III-2. Results of the NMR Integrations on the Product of the Reactions.

1) $Ph_2P—CH_2Cl + CH_3COOH \xrightarrow[H_2O]{}$

2) $Ph_2P—CH_2Cl + CD_3COOD \xrightarrow[D_2O]{}$

3) $Ph_2P—CH_2Cl + CH_3COOH \xrightarrow[D_2O]{}$

Reaction	Integration Values in mm. Ar	Alk	Proton Ratio Ar	Alk	Average(*) % error
1	179.75	53.35	10	2.985	-2.77
	193.3	54.75	10	2.815	
	178.55	52.65	10	2.945	
	222.35	63.80	10	2.84	
2	190.15	39.05	10	2.00	+2.98
	197.70	42.00	10	2.14	
	211.70	44.15	10	2.09	
	215.50	44.00	10	2.04	
3	392.90	125.00	10	3.18	+6.17
	206.5	66.05	10	3.18	

(*) % error was estimated as follows:

P=(Integration value of Aromatic Protons)/10

Q=(Integration Value of Alkyl Protons)/3(2)

$$\% \text{ error} = \frac{P-Q}{P} \times 100$$

and the resulting mixture was heated to 90-100° for 6 hr under an atmosphere of nitrogen. Acetic acid and the volatile products were removed under vacuum. The residue was treated with 10 ml of water and extracted with benzene.

The benzene layer was dried and evaporated to give 1.5g (37%) of an oily material that solidified on standing, m.p. 41-43° (clears at 45-45°). (49-50°) [122]. The nmr ($DCCl_3$) of (138) showed peaks at: τ=6.11 (4H, d, $^2J_{PCH}$=6.5 cps), τ=8.26 (3H, d, $^2J_{PCH}$=13.2 cps). Similar results were obtained with acetic acid-d_4. The amount of dueterium incorporation was estimated to be 0.86±0.069 atom/molecule. The lack of complete corporation of one atom of deuterium in this compound may be due to the decomposition of (129) to give HCl.

The Product Analysis of the Reaction Acetic Acid with tris-(chloromethyl)phosphine (129). Equivalent amounts of (129) and glacial acetic acid were mixed and sealed at 131° for 27 hr.. The nmr was reexamined and each peak was integrated. The peaks were identified as acetyl chloride and acetic anhydride by adding small amounts of pure acetyl chloride and acetic anhydride to the opened nmr tube and watching the respective peaks increase in intensity. (Acetyl Chloride τ=7.80, Acetic Anhydride τ=8.11).

A working curve was constructed by weighing known amounts of acetyl chloride and acetic anhydride and estimating the relative intensity of the peaks due to these compounds. The plot of Mole % composition by integration vs Mole % of acetic anhydride is shown in Fig. 1. The amount of acetic anhydride in the reaction mixture was estimated to be 8.4 mole % on the basis of this plot.

The rate of halofen exchange of the reaction:

$$Ph_2P(O) - CH_2Cl + I^- \quad Ph_2P(O) - CH_2I + Cl^-$$

was determined by the method of Conant [125]. A sample of 0.001 mole of chloromethyldiphenylphosphine oxide was weigned in an ampule. To this was

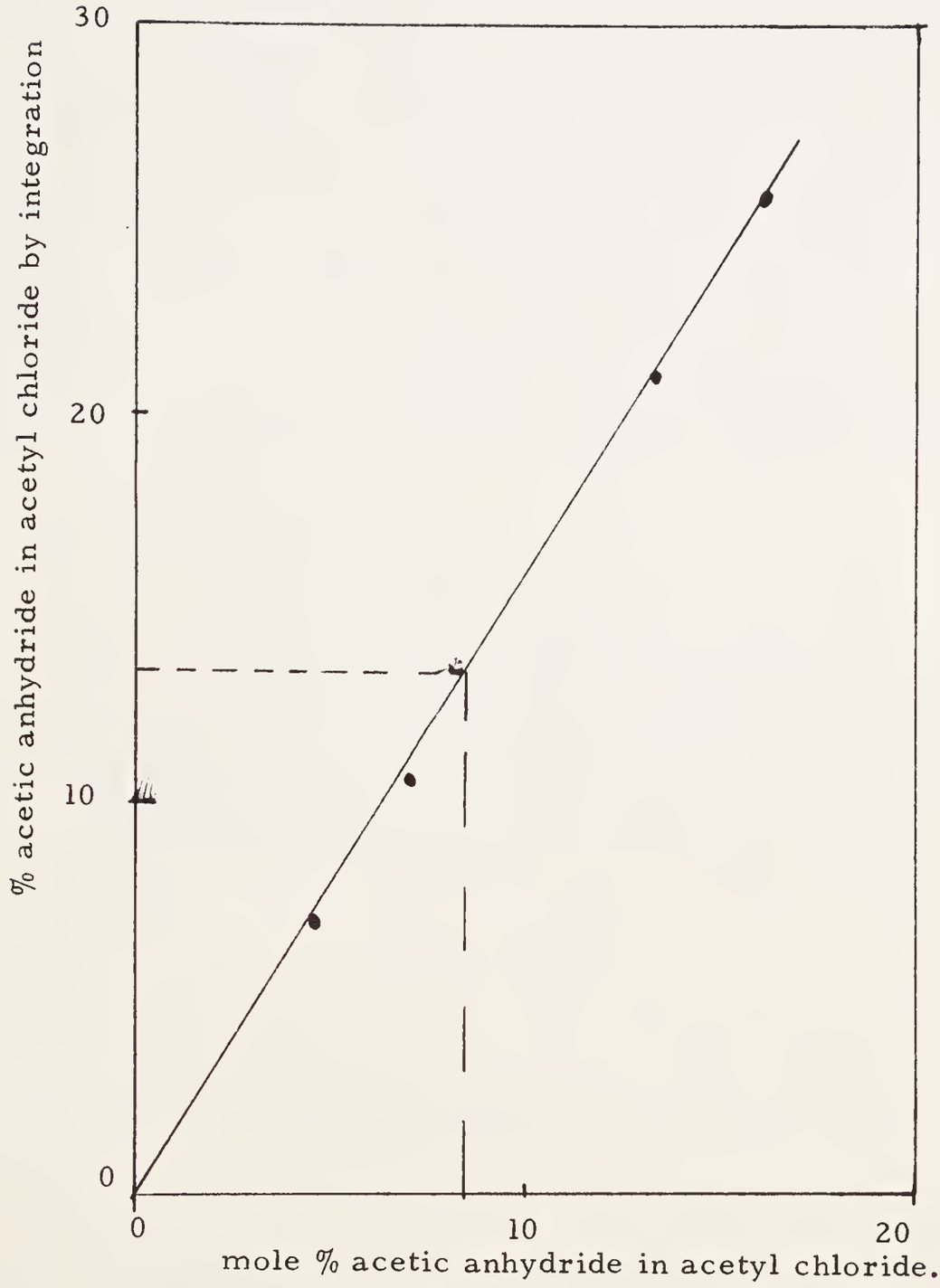


Fig. III-1. Working curve for the determination of concentration of acetic anhydride in acetyl chloride.

added 5 ml of 0.04 M potassium iodide solution acetone. The reactants were essentially unreactive at room temperature. The ampule was sealed and heated in a constant temperature bath at 80°. After a given length of time, the tube was removed from the bath and the contents of the tube were quantitatively transferred to a small separatory funnel containing a mixture of ice and concentrated HCl [132]. The mixture was extracted with three 5 ml portions of chloroform. The aqueous solution was transferred to an Erlenmeyer fork, a 5 ml portion of choroform was added and the mixture was titrated against 0.00301 N KIO_3 solution from the burette. The titration took about 10 min. and the end point was marked when the yellow color of the chloroform layer just disappeared. A blank titration was performed with 5 ml of 0.04 M potassium iodide in acetone. The rate constant for the reaction was calculated using the following formula by Conant [132]:

$$k = \frac{1}{t} \times 4b \log \frac{5-z}{5(1-z)}$$

where b=concentration of potassium iodide in moles per liter, z=the fraction of KI which has reacted in the time t measured in hr., the value of z is the difference in the actual and blank titrations divided by the blank titration. The table III-3 represents the values of the rate constants obtained for (115).

Table III-3. Kinetics of Halogen Exchange for the Reaction:

$$PH_2P(O)\text{-}CH_2Cl + I^- \rightarrow Ph_2P(O)\text{-}CH_2I + Cl^-$$

(115)

At 80°

#	Time hr.	Reading	k (Calcd.) 1. $m.^{-1}$ $hr.^{-1}$
1	193	3.5 ml	2.89×10^{-2}
2	295	2.0 ml	2.70×10^{-2}
3	365	1.1 ml	2.96×10^{-2}

Av. $k_2 = 2.85 \times 10^{-2}$ 1. m^{-1}. hr^{-1}.

n-BuCl	k_2	50°	0.0415 $1.m^{-1}$. hr^{-1}.
		60°	0.117
		80°	0.944 (extrapolated)

CHAPTER IV

NUCLEAR MAGNETIC RESONANCE STUDIES ON PHOSPHETANE DERIVATIONS

1. Introduction.

The development of organic chemistry in the last two decades is marked by the deluge of nmr data in the literature [133,134]. Although, most of these data concern ^{1}H and ^{19}F systems; both ^{31}P and ^{13}C (each with spin = 1/2) have received a considerable attention [135,136]. The chemical shifts and coupling constants provide a useful information of the various structural features and stereochemistry of the molecules. The ^{1}H and ^{19}F nuclei are monovalent and hence do not possess an intrinsic stereochemistry. The ^{31}P and ^{13}C nuclei on the other hand, because they are polyvalent, have stereochemistry due to substituents around them. Thus, nmr spectroscopy of molecules containing these nuclei provides an additional source of information.

^{31}P magnetic resonance spectroscopy has made a significant contribution to the early development of nmr spectroscopy [137]. This was primarily due to the fact that the isotope ^{31}P occurs with 100% natural abudance, which allowed for measurements, even with instruments of low resolution. As a result, the early development of nmr theory was not seriously hampered due to the inavailability of instruments of high resolution [137].

The routine use of a typical ^{31}P instrument is limited due to the low sensitivity of the phosphorus nucleus to nmr experiments, ca. 6.6% of that for proton at the same field [138]. This requires a high concentration of the samples. Such limitations have led to the development of techniques

by which chemical shifts and coupling constants for these nuclei can be calculated. The technique is commonly known as "nuclear Magnetic double resonance" or "heteronuclear spin decoupling" [139].

The technique mentioned above has had wide applications in the analysis of an nmr spectrum. The basic principle is that the multiplet structure arising from the coupling of certain nuclei can be eliminated by decoupling the spins of these nuclei from the remainder of the spin system [140]. As a result, a simplified spectrum is obtained. The technique of double resonance, therefore, is a valuable tool for the determination of coupling constants and theri relative signs [139, 141].

The method of double resonance has also been utilized to obtain chemical shifts of various nuclei, e.g., ^{13}C [141], ^{31}P [142] and ^{15}N [143]. The method was first employed by Royden [141] for determining the resonance frequency of $^{13}CH_3I$.

2. Results and Discussion.

The advantage of the above technique can be applied to the organophosphorus compounds in this investigation. Since ^{31}P chemical shifts can be obtained while observing the corresponding nmr spectrum, concentrated solutions are unnecessary. Further, most of the compounds in this investigation have moderately resolved nmr spectra and are readily interpretable [11].

The ^{31}P chemical shift of all the compounds were obtained by the method of Stothers [144]. The chemical shifts of some phosphetanes relative to 85% phosphoric acid are shown in table III-1.

Attempts have been made to correlate phosphorus chemical shifts with different parameters. Correlations based on electron donating or withdrawing effects of the substituents at phosphorus do not seem to exist in

the phosphorus compounds [137]. Attempts have also been made to correlate ^{31}P chemical, shifts with Taft σ^* values without success [137]. It may also be mentioned here that Taft correlations on the basicity of the phosphetanes have also been unfruitful [2]. The available evidence indicates that the chemical shifts of phosphorus nuclei depend on at least two parameters, namely; i) the ionic character of the bond, and ii) hyperconjugation of the protons [145]. The failure of Hammett and Taft correlations in these systems can be readily understood on the basis of the above variables. In any event, some correlations have been possible and have led to several generalizations [145,146]. Empirical equations for calculating ^{31}P chemical shifts in tertiary and secondary phosphines are shown below:

$$\Delta ppm = 62 - \sum_{n=1}^{3} \bar{O}n^{p}$$ for tertiary phosphines where $\bar{O}^{p}$ = empirically determined group contribution

$$\Delta Ppm = 99 - \sum_{n=1}^{2} \bar{O}^{p}$$ for secondary phosphines n=number of substituents

Good correlations are obtained by ploting the calculated vs. observed chemical shifts [145].

Grim and co-workers [147] reported a new parameter in which the effect of hyperconjugation was an important factor. The group contributions were calculated from the following relation:

$$Cr = 21 - 14\beta_c + 3T_c$$

where β_c and T_c are the number of β and Tcarbon atoms of a substituent, on phosphorus. An examination of the equation reveals that substituents of a α-hydrogen by a methyl group leads to a significant negative contribution to the chemical shift, i.e., leads to deshielding of the phosphorus nucleus. In the following equation:

$R_2\ddot{P} - CR_2H \qquad R_2\ddot{P}^- = CR_2\ H^+$

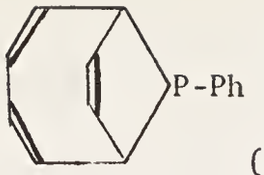
progressive substitution of hydrogens reduces the hyperconjugative shielding of the nucleus.

^{31}P chemical shifts of the several phosphetanes are shown in table 1. The calculated values based on Grim's group contributions are also shown where applicable. The plot of the calculated vs. observed chemical shifts fails to show adequate correlation (Fig. 1).

The effect of hyperconjugation, however, may be qualitatively used to provide a rationale for the observed phosphorus chemical shifts. Thus, compound (141) which has two hydrogens in the ring has the most shielded ^{31}P nucleus in the series investigated. Substitution of α-hydrogens by a methyl group leads to deshielding of the nucleus as anticipated, e.g., (141)> (17) , (140)> (142). Similar effects of hyperconjugation in (23) vs. (143) can also be seen. However, the hyperconjugative contribution due to the ring substituents in the molecule and that due to the exocyclic substituents are not necessarily parrallel, e.g., phosphorus in (140) with two α-hydrogens in the ring is significantly more shielded than that in (23) which has three α-protons in the exocyclic part of the molecule.

The effect of m- and p- substituents on the aromatic ring is not significant. Thus, chemical shifts for compounds (144), (145) and (146) are very similar to that for the unsubstituted phosphetane (41).

A very interesting feature of the table 1 is the chemical shift differences between the trans and the cis isomers of some of the phosphetanes: i.e., the cis isomer is more shielded than the trans. Katz [148] has reported 65 ppm difference in the two isomers of (147):

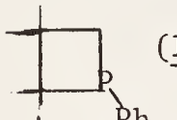
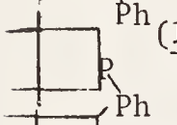
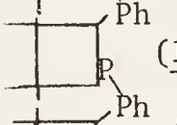
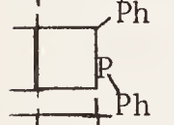
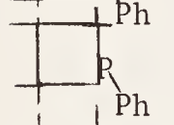
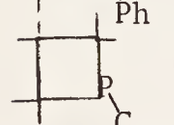
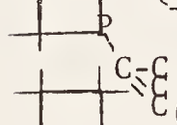
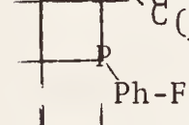
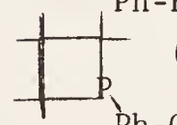
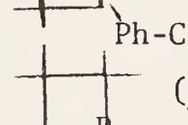


(147)

This, however, appears to be an isolated case. The dependence of chemical shifts of a heteronucleus on stereochemistry has been noted in ^{13}C nmr. Stothers [149] has shown that the carbinol carbons bearing axial and equatorial oxygen functions in derivatives of cis and trans 4-t-butylcyclohexanol have substantial chemical shift differences. The carbon possessing an axial substituent was shown to be 4-5 ppm more shielded than the one with an equatorial substituent:

Table IV-1. ^{31}P Chemical Shifts of Phosphetanes relative to 85% H_3PO_4.

$\delta_{ref}\ P(OCH_3)_3 = -140.5$

Compound	ν Sample cps	ν Ref cps	δ Correction	$\delta^{31}P$ ppm observed	Calcd.*
 (140)	6156	9338	+2.25	-5.8	-12
 (141)	6038	8867	+2.70	-21.4	-15
 (17)	6267	8870	+2.40	-31.0	-29
 (142)	5945	8747	+2.25	-23.0	-26
 (141)	6865 (trans)	8914	+2.03	-54.2	
	6389 (cis)	8914	+2.03	-36.6	-43
 (23)	5543	8225	+0.62	-29.5	-25
(143)	6783 (trans)	8204	+0.91	-81.3	
	6055 (cis)	8204	+1.48	-50.6	-69
 (144)	7655 (trans)	9683	+2.09	-55.0	
	7162 (cis)	9683	+2.13	-34.6	
 (145)	6094 (trans)	8174	+2.00	-53.0	
	5684 (cis)	8174	+2.00	-36.0	
 (146)	6347 (trans)	8419	+2.00	-53.2	
	5925 (cis)	8174	+2.00	-36.0	
 (48)	9453 (trans)	8765	+2.33	-165.5	
	8884 (cis)	8717	+2.30	-145.0	

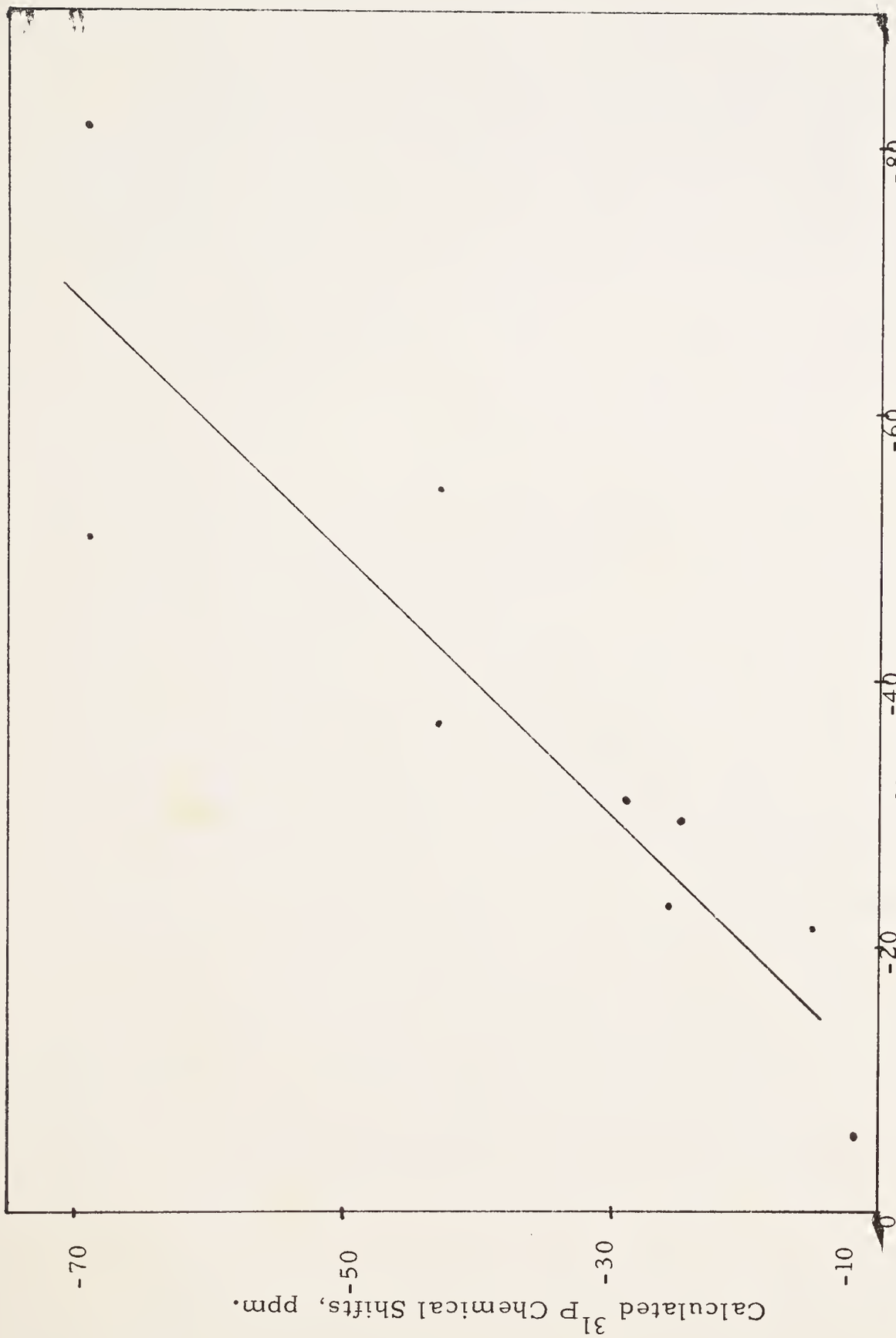
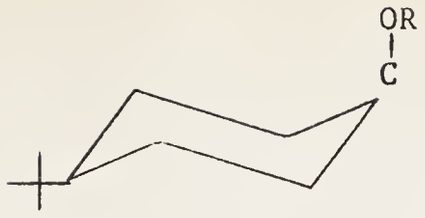
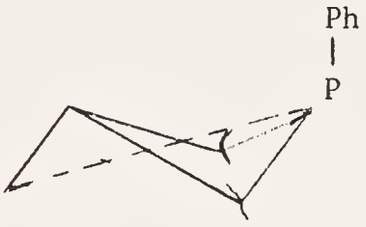


Fig. IV-1 . Plot of Calculated vs Observed ^{31}P Chemical Shifts of Phosphetanes.



The contribution to the chemical shift of the substituent not bonded to the nucleus is questionable, since the relative position of the nucleus with respect to the substituent does not change significantly (see also ref p. 154):



Thus, the differences of the chemical shifts in isomers must arise either from the substituents or the lone pair of electrons. In the case of phosphetane oxides and phosphetanium salts, no differences in ^{31}P chemical shifts was observed between the isomers. This leads one to conclude that the orientation of the lone pair of electrons is probably a major cause of the chemical shift difference between the isomers of phosphetanes. In any event, these differences in ^{31}P resonance in isomers (cis and trans) of phosphetanes are empirically useful in making isomer assignments.

Attempts to make correlations in phosphonium salts have been reported [150]. Once again, electron withdrawing or donating effects fail to give correlation with available data [150]. Hyperconjugative can be qualitatively used to rationalize the observed chemical shifts in some open-chain systems, but not enough data is available to give any quantitative predictability [150].

The qualitative correlation of ^{31}P chemical shifts in phosphetanium salts may also be attempted on the basis of hyperconjugation arguments. Thus, phosphorus in compound [150] is more shielded than in (27) as antici-

pated (table IV-2). Similar arguments, however, fail to hold for the exocyclic substituents in case of compounds (27), (94), and (149). The expected trend on the basis of hyperconjugation is:

(149)> (27)> (94)

where as the observed order is:

(27)> (94)> (149)

The chemical shifts of phosphinate esters are shown in Table IV-3. The values for various compounds are so close to each other, that correlations on the basis of hyperconjugation (or any other effect for that matter) can not be used.

Proton magnetic resonance spectroscopy has also provided a valuable tool for the stereochemical assignments in the phosphetane compounds [2,11], and has been successfully employed for following the stereochemical course of reactions of these compounds [26,33]. Fig. IV-2 shows a partial pmr spectrum of a mixture of isomeric chlorophosphetanes (48). The corner proton at position 3 in the trans isomer (1,Cl and 3-methyl, trans) (see p.16). is less shielded than that in the cis isomer. The assignment is consistent with the ^{31}P data. The corner proton with phosphorus in the cis isomer is observed. Since, in this case as well as in others phosphetanes for the corner proton, $^{3}J_{PCCH}$(trans) $^{3}J_{PCCH}$(cis) seems to hold the relation may be a good guide-line for the isomer assignments.

Another application of isomer assignments is possible in the phenylphosphetane (148). Cremer and Chorvat found that the compound did not isomerice on heating [2]. The assignment of the geometry of the 1,phenyl, 2-methyl relationship was not made. In light of the additional information below, a tentative assignment may be made.

Table IV-2. ^{31}P Chemical Shifts of Phosphetanium Salts Relative to 85% H_3PO_4. Reference $\delta P(OCH_3)_3$=140.5 ppm.

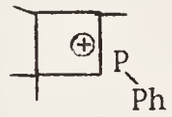
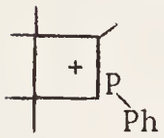
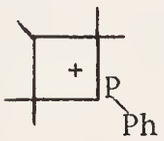
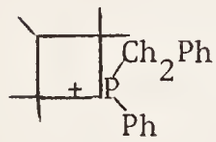
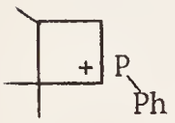
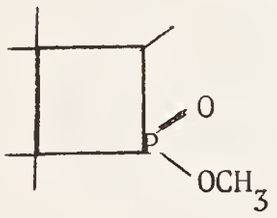
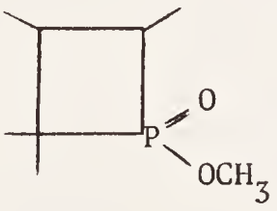
Compound	νSample cps	νReference	δCorrection	$\delta^{31}P$ ppm.
 (27)	4119	6097	+0.25	-58.65
 (148)	5491	7712	+0.77	-48.3
 (149)	7573	9485	+0.98	-61.8
 (94)	3926	5977	+1.12	-55.5
 (150)	7215	9560	+0.72	-43.0

Table IV-3. ^{31}P Chemical Shifts of Phosphinate Esters Relative to 85% H_3PO_4.δ Reference (CH_3PCl_2) = 191 ppm.

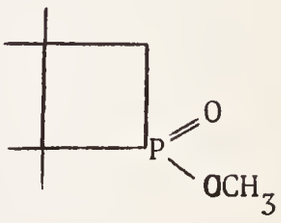
Compound	νSample	νReference	δCorrection	δ3/p Observed
(11)	5404	8840	-0.9	-50.5
(15)	5367	8850	-0.8	-48.5
(8)	5464	8874	-0.9	-49.8
(86)	5532	8895	-1.1	-53.7
(93)	5459	8887	-0.9	-50.8



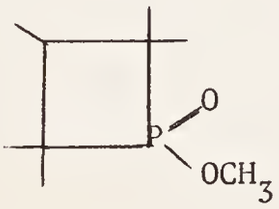
(8)



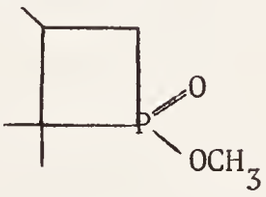
(11)



(15)



(86)



(93)

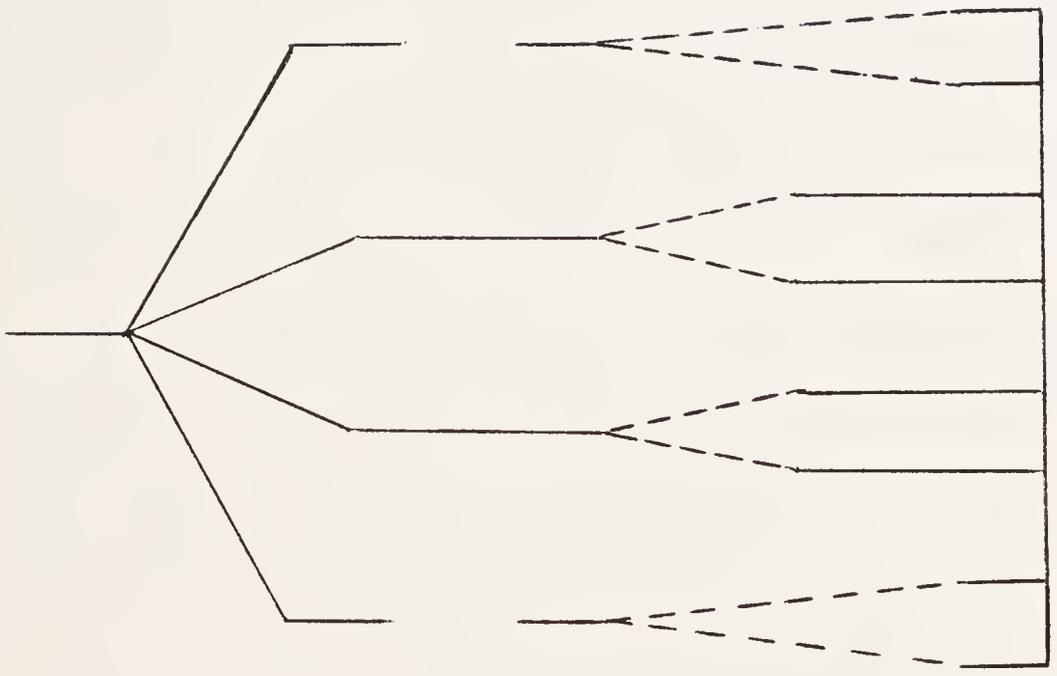
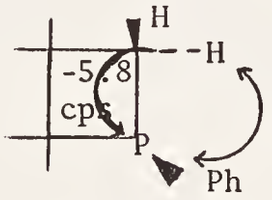


Fig. IV-2. Splitting pattern for the corner proton in chlorophosphetane (48). $^{3}J_{PCCH}$ (cis) = 1.25 cps, $^{3}J_{PCCH}$ (trans) = 2.50 cps.

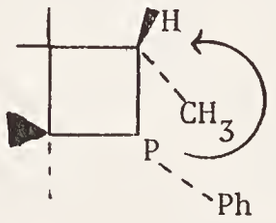
Gagnaire [151] has described the influence of bond orientation around phosphorus on the J_{PH} coupling constants in trivalent phosphorus compounds The dependance of the magnitude as well as the sign of the coupling constants on orientation has also been shown. Fig. IV-3 represents the curve of $^{2}J_{PCH}$ vs. f(∝) in which ∝ is the dihedral angle subtended by the two planes defined by the P, C and H atoms and by the C-P bond together with the three-fold axis of the bonds around phosphorus (assuming a regular pyramidal arrangement, with a bond angle value of 100° for all compounds.

On the basis of this curve, Gagnaire [152] has made the following geometrical assignment: in the case of phenylphosphetane (149):



(149)

The observed coupling constant $^{2}J_{PCH}$ in phenylphosphetane (148) is ±7 cps. This suggests that the phenyl group and the methyl group are on the same side of the ring. i.e., the phenyl and the methyl are **cis** as represented in the illustration below:



± 7 cps

(148)

3. Experimental.

The proton magnetic resonance spectra of the compound were obtained on a Varian A-60 instrument. For the decoupling experiment, a suitable peak for each compound in the pmr was observed while irradiating the sample with another frequency in the vicinity of 24.3 mcps provided by an HD-60A oscillator (NMR Specialties Co.). The frequency was modulated with an audio oscillator and was transmitted through the crystal, to the sample. De-

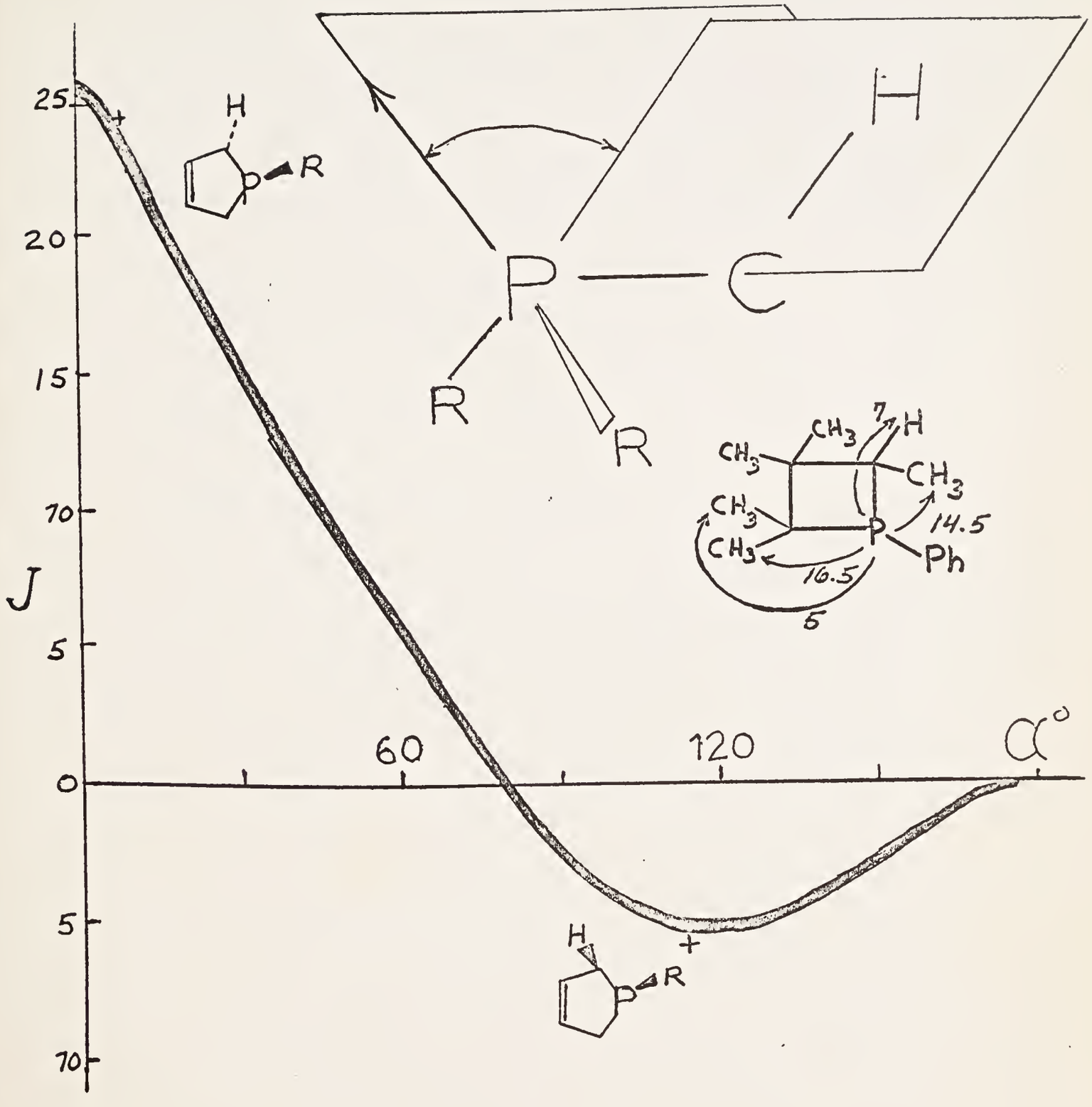

25
20
15
10
J
5
0
5
10
60
120
α°
H
R
P
C
H
R
R
CH3
CH3
CH3
CH3
P
Ph
H
14.5
16.5
5
H
R

Fig. IV-3.

coupling was evident from the collapse of the splitting pattern due to phosphorus, i.e., a doublet -- a singlet, etc.. The gain in the decoupler was minimized in order to reduce the error in the frequency measurement. The frequency of decoupling was observed in the counter while allowing a stream of dry nitrogen to cool the sample. This was necessary to overcome the heating effect during irradiation. The chemical shifts of the phosphorus nuclei were calculated using the following relations [144]:

$$\delta Sample = - \frac{\nu sample - \nu ref.}{24.3}$$

$$\delta Uncorrected = \delta sample - \delta ref.$$

$$\delta ppm = \delta uncorrected \pm \delta correction$$

correction in ppm is the difference in the chemical shifts of the hydrogen of the compound under investigation and the proton shift of the reference compound. The Correction factor δcorrection is to be added or subtracted depending upon whether the proton signal (used for decoupling) of the sampel is at a higher or lower field than the signal for the reference material [144].

REFERENCES

1. S. E. Cremer and R. J. Chorvat, Tetrahedron Lett., 413 (1968.

2. R. J. Chorvat, Ph.D. Thesis, Illinois Institute of Technology, Chicago, Illinois, 1968.

3. G. Markl, Angew. Chem. Internat. Ed. Engl., 4, 1023 (1965).

4. G. M. Kosolapoff and R. F. Struck, J. Chem. Soc., __, 3739 (1957).

5. R. I. Wagner, U.S. Patent 3,086,053 (1963); Chem. Abstr., 59, 10124 (1963).

6. R. I. Wagner, U.S. Patent 3,086,056 (1963); Chem. Abstr., 60, 559 (1964).

7. R. I. Wagner, L. D. Freedman, H. Goldwhite and D. G. Rowsell, J. Amer. Chem. Soc., 89, 1102 (1967).

8. M. Green, J. Chem. Soc., 541 (1965).

9. S. E. Cremer, Private Communication.

10. J. J. McBride, Jr., E. Jungermann, J. V. Killhefer and R. J. Clutter, J. Org. Chem., 27, 1833 (1962).

11. S. E. Cremer and R. J. Chorvat, J. Org. Chem., 32, 4066 (1967).

12. T. A. Zyablikova, A. R. Panteleeva and I. M. Shemegron, Izvest. Akad. Nauk S.S.S.R. Ser. Khim., 373 (1969) (Russ).

13. D. Berglund and D. W. Meek, J. Am. Chem. Soc., 90, 518 (1968).

14. C. H. Chang, Ph.D. Thesis, Illinois Institute of Technology, Chicago, Illinois (1969).

15. A. M. DeRoos and H. J. Toet, Rec. Trav. Chim. Pays-Bas, 78, 27 (1959).

16. S. E. Cremer and R. J. Chorvat, Tetrahedron Lett., 413 (1968).

17. S. E. Cremer, Chem. Commun., 1132 (1968).

18. S. Trippett and W. Hawes, J. Chem. Soc., C, 1465 (1969).

19. R. O. House, "Modern Synthetic Reactions", W. A. Benjamin, New York, N. Y. (1965).

20. C. S. Marvell and L. A. Brooks, J. Am. Chem. Soc., 63, 2630 (1941).

21. R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry", Monograph 6, Academic Press, New York, N. Y. (1965).

22. J. Hine, "Physical Organic Chemistry", McGraw-Hill, New York, N. Y., (196).

23. L. Horner, H. Hoffmann and H. G. Wippel, Chem. Ber., 91, 64 (1958).

24. K. Sasse in "Methoden Der Organischen Chemie", Vol. XII, Part I, ed. by E. Muller, George Thieme Verlag, Stuttgard, (1963). p. 239.

25. L. Horner and W. D. Balzer, Tetrahedron Lett., 1557 (1967).

26. S. E. Cremer, R. J. Chorvat, C. H. Chang and D. W. Davis, Tetrahedron Lett., 5799 (1968.

27. L. M. Trefonas and C. Moret, J. Am. Chem. Soc., 91, 2255 (1969).

28. M. J. Gallagher and I. D. Jenkins, "Topics in Stereochemistry", Vol. 3, N. L. Allinger and E. L. Elliel, Ed., John Wiley and Sons, Inc., New York, N. Y., (1 68).

29. D. W. Denney and N. G. Adin, Tetrahedron Lett., 2569 (1966).

30. C. N. Caughlan and M. Haque, Chem. Commun., 1228 (1968).

31. C. N. Caughlan, Private Communication.

32. M. Haque, Private Communication.

33. S. E. Cremer and B. C. Trivedi, J. Am. Chem. Soc., 91, 7200 (1969).

34. K. Bergesen, Acta. Chem. Scand., 21, 1587 (1967).

35. F. H. Westheimer, Accounts Chem. Res., 1, 70 (1968).

36. E. Uhing, K. Rattanbury and L. Maier, J. Am. Chem. Soc., 83, 2299 (1961).

37. H. E. Ulmer, L. C. D. Greenweghe and L. Maier, J. Inorg. Nucl. Chem., 20, 82 (1961).

38. S. Trippett and D. J. H. Smith, Chem. Commun., 855 (1969).

39. R. Collin and G. Shreder, German Patent, 1,056,606 (1958), Chem Zent., 130, 17390 (1959).

40. H. L. Roberts in "Inorganic Sulfur Chemistry", G. Nickless, Ed., Elsevier Publ Co., Amsterdam (1968) Chapter 12.

41. M. S. Kharasch and H. C. Brown, J. Am. Chem. Soc., 61, 2142 (1939).

42. Zh. L. Eutikhov, N. A. Razumova and A. A. Petrov, Proc. Acad. Sc. USSR (English Trnas.) 181, 746 (1968).

43. W. E. Backman and C. H. Boatner, J. Am. Chem. Soc., 58, 2194 (1936).

44. A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus", Monograph 5, Elsevier Publ. Co., Amsterdam, (1967).

45. R. J. Gillespie, J. Chem. Soc., 1002 (1962).

46. R. J. Gillespie, J. Chem. Soc., 4672 (1963).

47. H. Braun and P. Pinnow, Z. Physik. Chem., B-25, 239 (1937).

48. F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry", Interscience, New York, N. Y. (1962).

49. K. W. Hansen and L. S. Bartell, Inorg. Chem., 4, 1775 (1965).

50. H. S. Gutowsky and A. D. Liehr, J. Chem. Phys., 20, 1652 (1952).

51. H. S. Gutowsky, D. W. McCall and C. P. Slichter, J. Chem. Phys., 21, 279 (1953).

52. R. R. Holmes, J. E. Griffith and R. P. Carter, J. Chem. Phys., 41, 863 (1964).

53. R. R. Holmes, J. E. Griffith and R. P. Carter, Inorg. Chem., 3,1748 (1964).

54. F. Ramirez, W. C. Hamilton and S. J. LaPlaca, J. Am. Chem. Soc., 87, 127 (1965).

55. R. S. Berry, J. Chem. Phys., 32, 933 (1960).

56. J. J. Downs and R. E. Johnson, J. Am. Chem. Soc., 77, 2098 (1955).

57. J. R. VanWazer and J. H. Letcher, J. Chem. Phys., 45, 2926 (1966)

58. E. L. Muetterties, W. Mahler and R. Schmutzler, Inorg. Chem., 2, 613, (1963).

59. K. W. Hansen and L. S. Bartell, Inorg. Chem., 4, 1777 (1965).

60. E. L. Muetterties, W. Mahler, K. J. Parker and R. Schmutzler, Inorg. Chem., 3, 1298 (1964).

61 P. M. Triechel, R. A. Goorich and S. B. Pierce, J. Am. Chem. Soc., 89, 2017 (1967).

62. R. S. Drago and P. C. VanderVoorn, J. Am. Chem. Soc., 88, 3255 (1966).

63. H. Bent, Chem. Rev., 61, 275 (1961).

64. D. P. Craig, R. S. Nyholm, A. Maccoll and L. E. Sutton, J. Chem. Soc., 332 (1954).

65. R. J. Gillespie, Can. J. Chem., 38, 818 (1960), 39, 318 (1961).

66. R. J. Gillespie, J. Chem. Soc., 332 (1954).

67. R. Schmutzler, Inorg. Chem., 2, 613 (1963).

68. R. Alver and B. H. Holtedahl, Acta. Chem. Scand., 21, 359 (1967).

69. W. N. Lipscomb and Y. H. Chiu, J. Am. Chem. Soc., 91, 4150 (1969).

70. F. H. Westheimer and R. Kluger, J. Am. Chem. Soc., 91, 4143 (1969).

71. D. J. Cram, Private Communication.

72. J. D. Dunitz and V. Prelog, Angew. Chem. Internat. Ed. Engl. 7, 725, (1968).

73. K. Mislow, K. E. DeBruin, K. Naumann and G. Zon, J. Am. Chem. Soc., 91, 7031 (1969).

74. F. H. Westheimer and F. Covitz, J. Am. Chem. Soc., 85, 1773 (1963).

75. F. H. Westheimer and P. C. Haake, J. Am. Chem. Soc., 83, 1102 (1961).

76. D. B. Boyd, J. Am. Chem. Soc., 91, 1200 (1969).

77. F. H. Westheimer and E. A. Dennis, J. Am. Chem. Soc., 88, 3432 (1966)

78. G. Aksnes and K. Bergesen, Acta, Chem. Scand., 20, 2508 (1966).

79. D. Samuel and B. L. Silver, Advan. Phys. Org. Chem., 3, 123 (1965).

80. F. H. Westheimer, F. Kerst, D. G. Lee and E. A. Dennis, J. Amer. Chem. Soc., 89, 3918 (1967).

81. F. H. Westheimer, F. Covitz, E. A. Dennis, R. Kluger and L. David Williams, J. Am. Chem. Soc., 91, 6066 (1969).

82. R. F. Hudson and M. Green, Proc. Chem. Soc., 307 (1962).

83. R. F. Hudson and M. Green, Angew. Chem. Internat. Ed. Engl. 2, 17, (1963).

84. J. Hine, J. Org. Chem., 31, 1236 (1966).

85. F. O. Rice and E. Teller, J. Chem. Phys., 6, 489 (1938), 7, 199 (1939).

86. S. Trippett and W. Hawes, Chem. Commun., 577 (1968).

87. F. G. Bordwell and G. D. Cooper, 73, 5184 (1951).

88. K. Bergesen, Acta. Chem. Scand., 21, 1587 (1967).

89. A. A. Forst and R. G. Pearson, "Kinetics and Mechanism", John Wiley and Sons, Inc., New York, N.Y. (1961).

90. A. W. Hoffmann, Ann., 78, 253 (1851).

91. A. W. Hoffman, Ber., 14, 459, 659 (1881).

92. A. W. Hoffman, Ann., 79, 11 (1851).

93. A. W. Hoffmann, and A. Cahours, Ann., 104, 1 (1857).

94. E. A. Letts and N. Collie, Trans. Roy. Soc. Edinb.,30, 181 (1885).

95. J. Meisenheimer, Ann., 449, 218 (1926).

96. C. K. Ingold and G. W. Fenton, J. Chem. Soc., 2342 (1929).

97. J. Meisenheimer, Ber., 44, 356 (1911).

98. C. K. Ingold and L. Hey, J. Chem. Soc., 531 (1933).

99. H. L. Horner, H. Hoffmann, H. G. Wippel and G. Hassel, Chem. Ber., 91, 52 (1958).

100. W. E. McEwen, K. F. Kumli, A. Blade-Font, M. Zanger and C. A. VanDer Werf, J. Am. Chem. Sco., 86, 2378 (1964).

101. W. E. McEwen, K. F. Kumli and C. A. VanDer Werf, J. Am. Chem. Soc., 81, 3806 (1959).

102. W. E. McEwen, G. Axelrad, M. Zanger, and C. A. VanDer Werf, J. Am. Chem. Soc., 87, 3948 (1965).

103. S. Trippett, J. R. Corfield and J. R. Shutt, Chem. Commun., 789 (1969).

104. S. E. Cremer, R. J. Chorvat and B. C. Trivedi, Chem. Commun. 769 (1969).

105. W. E. McEwen, K. F. Kumli and C. A. VanDer Werf, J. Am. Chem. Soc., 81, 3805 (1959).

106. K. L. Marsi, J. Am. Chem. Soc., 91, 4724 (1969).

107. K. Mislow, K. Naumann and P. D. Henson, J. Am. Chem. Soc., 91, 5646, (1969).

108. G. Aksnes and K. Bergensen, Acta. Chem. Scand., 19, 931 (1965).

109. G. Aksnes and J. Songstad, Acta. Chem. Scand. 16, 1426 (1962).

110. G. Markl, Z. Naturforsch, 18b, 84 (1963).

111. K. A. Petrov, V. A. Parshina and V. A. Gaidaniak, Zhur, Khim., 31, 3411 (1961).

112. S. A. Buckler and M. Epstein, Tetrahedron, 18, 1231 (1962).

113. S. A. Buckler and V. P. Wystrach, J. Am. Chem. Soc., 83, 168 (1961).

114. H. Hellmann and Jorg Bader, Tetrahedron Lett., 724 (1961).

115. K. D. Berlin and M. E. Peterson, J. Org. Chem. 32, 125 (1967).

116. L. M. Yagupolskii and P. A. Yufa, J. Gen. Chem. USSR. Engl. 28, 2880 (1958).

117. M. S. Newman, J. R. Leblanc, H. A. Karnes and G. Axelrad, J. Am. Chem. Soc., 86, 868 (1964).

118. D. E. McGreer, Can. J. Chem., 38, 1638 (1960).

119. C. H. DePuy, G. M. Dappen, K. L. Eilers and R. A. Klein, J. Org. Chem., 29, 2813 (1964).

120. N. Krutzkamp, E. Schmidt-Samoa and K. Herberg, Angew Chem. 77, 1138 (1965).

121. M. Hojo and Z. Yoshida, J. Am. Chem. Soc., 90, 4596 (1968).

122. M. I. Kabachnik and E. N. Tsvetov, Proc. Acad. Sc. USSR., Chem. Sec., Engl. 143, 211 (1962).

123. C. E. Griffin, E. H. Uhing and A. D. F. Toy, J. Am. Chem. Soc., 83, 2299 (1961).

124. C. E. Griffin, E. H. Uhing and A. D. F. Toy, ibid, 87, 4757 (1965).

125. H. Goldwhite, B. Fontal and D. G. Rosell, J. Org. Chem., 31, 2424 (1966).

126. K. Moedritzer, J. Am. Chem. Soc., 83, 4381 (1961).

127. A. Aguiar and D. Daigle, J. Am. Chem. Soc., 86, 2299 (1964).

128. J. Meisenheimer, J. Casper, M. Horing, W. Lauter, L. Lichtenstadt and W. Samuel, Ann., 449, 213 (1926).

129. A. E. Arbuzov, J. Russ. Phys. Chem. Soc., 42, 549 (1910).

130. D. E. Seyferth, D. E. Welch, and J. K. Heeran, J. Am. Chem. Soc., 86, 1100 (1964).

131. H. Hoffmann, J. Am. Chem. Soc., 52, 2995 (1930).

132. J. B. Conant and W. R. Kirner, ibid., 46, 232 (1924).

133. J. A. Popple, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, N.Y., (1959).

134. F. A. Bovey, "NMR Data Tables for Organic Compounds", Vol. 1, Interscience , New York, N.Y. (1967).

135. J. W. Emsley , J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Pergamon, Oxford, (1966).

136. F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy", Academic Press, New York, N.Y., (1969).

137. "Topics in Phosphorus Chemistry", Vol. 5, ^{31}P NMR, Academic Press, New York, N.Y., (1967).

138. P. C. Lauterber, "Nuclear Magnetic Resonance Spectra of Elements Other Than ^{1}H and ^{19}F in Determination of Organic Structures by Physical Methods", Vol. 2, F. C. Nachod and W. D. Phillips, ed., Academic Press, New York, N.Y., (1962).

139. D. Baldeschweiler and E. W. Randall, Chem. Rec., 81 (1963).

140. F. Bloch, Phys. Rec., 102, 104 (1959).

141. V. Royden, ibid, 96, 543 (1954).

142. J. D. Baldeschweiler, J. Chem. Phys., 36, 152 (1962).

143. D. W. Turner, J. Chem. Soc., 847 (1962).

144. J. B. Stothers and J. R. Robinson, Cand. J. Chem., 967 (1964).

145. S. O. Grim, and W. McFarlane, Nature, 208, 995 (1965).

146. L. Maier, Helv. Chim. Acta., 49, 1718 (1966).

147. S. O. Grim. W. McFarlane and E. F. Davidoff, J. Org. Chem. 32, 781, (1967).

148. T. J. Katz, C. R. Nicholson and C. A. Reilly, J. Am. Chem. Soc., 89, 4301 (1967).

150. S. O. Grim, W. McFarlane, E. F. Davidoff and T. J. Marks, J. Phys. Chem., 70, 581 (1966).

151. D. Gagnaire, J. P. Albrand and J. B. Robert, Chem. Commun. 1469 (1968).

152. D. Gagnaire, J. P. Albrand, J. Martin and J. B. Robert, Bull. Soc. Chim. Fr., 40 (1969).

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Stereochemistry of Nucleophillic Attack at a Phosphinate Ester. S.E. Cremer and B.C. Trivedi, J. Am. Chem. Soc., 91, 7200 (1969).

The Chemistry of Phosphetanium Salts. S.E. Cremer, R.J. Chorvat and B.C. Trivedi, Presented at the Third Great Lakes Regional Meetings, American Chemical Society, Dekalb, Illinois, June 1969.

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